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The American Heart Journal

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The American Heart Journal

VOL. III AUGUST, 1928 No. 6

Original Communications

THE HEART IN INFECTION*

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NEW YORK, N. Y.

THE subject assigned for this paper recognizes that heart disease is rarely an affection of the heart exclusively, but rather only a part of a general systemic malady. In both its anatomy and physiology the heart has unique features which require consideration, but too close attention to them without due regard to the general problems of the biology of infection and degeneration may have a deterring rather than a beneficial effect.

It has become customary to divide heart diseases roughly into two general types: infectious and degenerative. The first are thought to exert their baneful influence largely during the first four decades of life, and the second class during the remainder. Vital statistics, indeed, confirm this impression; and a study of the form and function of tissues during the afternoon of life leaves little doubt of the importance of the alterations normally occurring in senescence as playing an important rôle in the production of cardiac diseases. But the age-linked features of these later alterations in structure may have blinded us somewhat to the relationship between infection and degeneration. Indeed some recognition of this relationship has been gained from the construction of actuary statistics, where their proper evaluation is a matter of dollars and cents. But only as the study of pathology becomes more and more a correlation of distant as well as immediate cause and effect, will there emerge a recognition of the true relationship of infection during the early years of life to late degenerations.

The effect of any infection upon the heart depends upon at least two factors: the nature of the infection and the reaction of the heart to that particular infection. The heart, being a complex organ, in turn shows different effects according as one or another of its component parts is involved. The heart, moreover, suffers a double insult both as

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a direct result of bacterial injury and as an indirect result of disturbed circulation; hence a vicious circle is quickly established in a cardiac infection. We must, therefore, keep these complicating factors in mind, for the result of even the simplest injury from bacteria is much more complicated than we imagine when we reduce the various elements to simple terms.

Again, we must recognize our comparative ignorance as to how the myocardium reacts to noxious agents. For example, we do not know to what extent or in what direction edema per se influences the various functions of the heart muscle: Does it increase or decrease irritability, contractility, or conductivity? Does it increase one and decrease another? What is the synergic or antagonistic result of these factors? Does mild prolonged irritation from infection lead to hypertrophy, or is hypertrophy only a response to a demand for increased work? Until we are able to give a positive answer to many such questions our discussions will, necessarily, have much of a hypothetical character.

We are in possession of enough data, however, to sketch at least rough outlines of many features of infectious heart diseases. At times it is necessary to obtain information concerning some factors from a direct study of infectious agents in parts of the body permitting direct examination, hence more accurate analysis. We must also resort to information gained from experimentation on lower animals, though in this respect, it must be confessed, we have obtained relatively little direct knowledge, in so far as infection of the heart is concerned. Aside from the type of heart involvement found in diphtheria and that of subacute bacterial endocarditis, we are unable to reproduce with any degree of regularity in lower animals the various pictures of cardiac infection that we encounter in man. Comparative experimental investigations, therefore, have yielded more direct information from the standpoint of physiology than from that of infection.

Keeping reservations of this nature in mind we shall base our discussion upon types of reaction in certain infections, rather than attempt to cover all of the features of infectious heart disease. A satisfactory picture of the various forms of cardiac injury from bacteria can probably be most clearly presented by using as examples the following diseases: diphtheria, scarlet fever, rheumatic fever, subacute bacterial endocarditis, syphilis, and septicopyemia.

DIPHTHERIA

In diphtheria the simplest picture of cardiac injury is seen. The heart is poisoned by the toxin produced at a distance, for it has been shown that all of the characteristic histological alterations found in the heart in fatal cases of diphtheria can be reproduced experimentally by injecting animals with bacteria-free diphtheria toxin.

The essential alteration is a degeneration of the muscle fibers, variously described as waxy, hyaline, and fatty; the differences recorded could no doubt be reconciled if variations in strength of toxin and time of action were considered. But injury to the parenchyma is quickly followed by interstitial response with edema, accumulations of wandering cells and proliferation of fixed connective-tissue elements. All of this secondary picture may be considered an effort to remove the débris of the irreparably damaged parenchyma and to repair the injury in so far as possible. Warthin[1] describes muscle regeneration beginning in the degenerated muscle fibers, and attributes the apparently efficient functional recovery seen in most cases of diphtheritic carditis to a fairly complete regeneration of the myocardium.

While the endocardium is grossly normal and verrucous endocarditis is rarely, if ever, a complication of diphtheria, both Baldassari[2] and Czirer[3] have described focal lesions in the endocardial and subendocardial tissues of the mitral valves. Even though endocardial injuries occur, it is evident that recovery usually takes place without permanent damage to these structures. Indeed, one of the most striking peculiarities of the diphtheritic heart is the disproportion between the degree of functional disturbance at the time of the acute attack and the small amount of residual organic or functional crippling.[4] During the acute stages the injury is made evident by marked myocardial weakness, and also by various types of cardiac irregularity, which in recent times have been proved to be due to ectopic beats, nodal rhythm, heart-block, and occasionally to auricular fibrillation. Probably in no other disease except rheumatic fever is it possible to demonstrate involvement of the conduction system so frequently by physiological methods of investigation. Histopathological proof of such involvement has also been adduced.

The patchy distribution of the degeneration, which has been demonstrated histopathologically, explains the possibility of recovery, for enough efficiently functioning myocardium usually remains to permit life to continue until reparative processes have progressed to a point where normal bodily function may be resumed. Even in severely poisoned hearts Edmonds and Cooper[5] have demonstrated that the muscle and conduction system can respond in a normal manner to drugs. The ultimate outcome in any given case doubtless depends upon the ratio of uninjured to injured muscle, and the difficulty encountered at the bedside is to estimate this ratio, for upon it rest both treatment and prognosis.

SCARLET FEVER

The different cardiac complications of scarlet fever, although comparatively infrequent, illustrate the various forms of cardiac injury resulting from infection more clearly than does any other single dis-

ease. For purposes of discussion these complications may be classified as (1) toxic; (2) allergic; (3) septicopyemic. The toxic cardiac symptoms closely resemble those found in diphtheria. They come on shortly after the initial defervescence, are often accompanied by bradycardia, and are characterized by signs of cardiac weakness. Usually there is little, if any, fever and very mild evidence of general intoxication. If the patient remains flat in bed he may give slight, if any, evidence of cardiac weakness, while, on the other hand, if he assumes the sitting or standing posture there occur dizziness, weakness, and other signs of an insufficient heart. Escherich and Schick,[6] who designate this condition as myasthenic, state that it practically never has a fatal outcome; hence histopathological descriptions are lacking. The similarity of the early symptoms of scarlet fever to those of diphtheria and the possibility of neutralization of the so-called scarlatinal toxin with an antitoxic serum, moreover, make plausible the hypothesis that this peculiar myasthenia cordis is due to a direct toxic action of a poison on the heart muscle.

The cardiac complication usually placed among the allergic manifestations of the disease is verrucous endocarditis, probably better called valvulitis. Schick[6] advanced the theory that the complications occurring from the end of the second to the sixth week after the onset of scarlet fever and with greatest frequency about the twentieth day are allergic in nature. This group includes adenopathy, recurring angina, nephritis, arthritis and occasionally simple endocarditis; they are always accompanied by fever. Nicoll[7] states that endocarditis is practically always a complication of arthritis and designates it a "complication of a complication." The assumption that both are manifestations of a common causative condition would, however, be more logical. Escherich and Schick attribute all of these symptoms to an allergic state which develops as the result of the prolonged action of the causative agent of scarlet fever in the body. At the time of their publication the etiological rôle of the Streptococcus scarlatinae was not established, but today we can assume with a fair degree of assurance that the stimulus to the development of this hypersensitive state is a streptococcus.

Hitchcock and I have been able to induce a condition of marked hypersensitiveness in rabbits by inoculating them intracutaneously with minute doses of hemolytic streptococci. Zinsser and Grinnell[8] and Mackie and McLachlan[9] have sensitized guinea pigs with both toxin and intact cells of streptococcus scarlatinae. Dochez and Stevens[10] have furthermore shown that two types of hypersensitiveness can be induced in rabbits by repeated injections over long periods with Streptococcus erysipélatis toxin. The first to appear is neutralizable with an antitoxic serum; the second is not so neutralizable, and when present can be demonstrated by testing with filtrates from a

variety of streptococci. Their work can be brought into relationship with both early and late clinical manifestations of scarlet fever. The early symptoms may be considered as evidence of hypersensitiveness to the toxin; the later ones as hypersensitiveness to the whole bacteria or to some other bacterial product. A series of scarlet fever patients should, however, be tested from this point of view before it can be definitely established.

Another hypothetical angle from which to view scarlatinal carditis in that these late allergic phenomena occur in those scarlet fever patients who are already partially hypersensitive to streptococci and that the added stimulus resulting from the scarlatinal infection increases the already existing allergy to a point where clinical symptoms are elicited. The well-known liability of a patient with quiescent rheumatic endocarditis to develop a relapse of rheumatic carditis following an attack of scarlet fever could be explained on these grounds. This liability has been recently emphasized by Hector.[11]

Since Romberg's[12] histopathological description of myocarditis in the different infectious diseases there has been much discussion of the relation of these structural changes to the clinical symptoms, and the heart in scarlet fever has not escaped consideration. The resemblance between late sequelae of scarlet fever and of rheumatic fever has directed the attention of pathologists toward a comparison of the microscopic picture in the two diseases. Schmorl[13] in 1914 stated that he had found lesions closely resembling Aschoff bodies in the heart of a scarlet fever patient. Stimulated by this finding, Fahr[14] made a detailed study of the myocardium in eight fatal cases of scarlet fever, as a result of which he concluded that the myocardial alterations in this disease resembled those of rheumatic fever more closely than they did those of any other infectious disease. He described them as perivascular granulomas, made up of proliferative cells from the perivascular adventitia; cells which were basophilic and stained red with pyronin. No giant cells were found, but myolysis of neighboring muscle fibers was often present. Thus, absence of giant cells and smaller size of the lesions were the chief features differentiating these lesions from those of rheumatic myocarditis. In certain cases of rheumatic carditis, on the other hand, interstitial myocardial foci were found indistinguishable from those of scarlet fever. Fahr mentions that the age of the lesions may be of significance but leaves the determination of this question open for future studies. He states that the valves in these hearts were normal but that focal thickening of the mural endocardium was present in four out of nine cases. Czirer,[3] on the other hand, described microscopic focal valvular lesions in thirteen cases of scarlet fever, and attributed later changes, often found at autopsy, to these earlier focal injuries. While it is evident

that the whole subject requires additional study, these investigations indicate the many elements of similarity between the heart in scarlet and rheumatic fevers.

The septicopyemic type of cardiac complication occurs in those rare instances where the Streptococcus scarlatinae becomes implanted and grows on the heart valve. It is an accident comparable to other forms of malignant endocarditis, and only related to scarlet fever because hemolytic streptococci in general have the capacity for producing this type of valvular disease.

RHEUMATISM

Heart involvement in rheumatic fever has interested pathologists and clinicians for over a century. Early the close relationship between verrucous endocarditis, pericarditis, and what was then called acute articular rheumatism was well established, and the relationship of acute rheumatic endocarditis to chronic valvular disease was fixed. Following the description by Aschoff[15] and by Geipel[16] of the peculiar submiliary nodules in the myocardium which now bear the former's name, the attention of both pathologists and clinicians was turned chiefly toward the myocardium and conduction system. But in recent years with a more extensive study of the general pathology of the disease, we are realizing that the pictures simply of the myocardial Aschoff body and of verrucous endocarditis are not sufficient to explain all of the damage caused by rheumatic fever. Indeed, we know that they represent only two reactions, to which other types of tissue response must be added if we are to have a satisfactory conception of the pathological evolution and functional disurbance seen at various periods of the disease.

Even before Aschoff's discovery of the specific submiliary nodule, the Leipzig school[17] had emphasized the importance of interstitial myocarditis in causing the symptoms referable to the heart in various common infectious diseases; but Aschoff and Tawara[18] a few years later strongly refuted the argument that all of the symptoms of myocardial weakness could be explained on the basis of the interstitial myocarditis in typhoid fever and scarlet fever, or by the presence of submiliary nodules in the rheumatic heart. In this same period the views of Poynton and Paine[19] concerning the etiological rôle of the Streptococcus rheumaticus were being advanced; and simultaneously numerous observers, among whom Schottmüller[20] and Libman[21] were most prominent, were establishing definitely the rôle of various strains of nonhemolytic streptococci in the production of subacute bacterial endocarditis. In the meantime physiological methods had claimed the attention of most investigators in the study of heart disease, and because in some instances a correlation of certain definite functional disturbances with lesions of the conduction system could be shown, there

arose a hope that most of the problems of cardiac disease were to be solved by the application of physiological and pathological data already available. With the passing of years, however, came the realization that much more information was required before a solution of the problem was in sight, and recently a large number of investigators have been directing their attention to various phases of rheumatic heart disease.

So far as we can determine, the earlier proponents of the etiological rôle of nonhemolytic streptococci in rheumatic fever never advanced a satisfactory hypothesis to explain the difference in the clinical and pathological pictures seen in this disease and that of subacute bacterial endocarditis. In fact most of the experimental evidence pointed to the ease of producing experimentally subacute bacterial endocarditis and the difficulty of reproducing any tissue changes at all comparable to those found in rheumatic fever patients. The diverse cultural and immunological characteristics of the strains of streptococci recovered by different workers added to the difficulty of bringing them into causative relationship with a disease which seemed to be such a definite clinical entity.

In our own clinical studies we had become more and more impressed with many points of resemblance between rheumatic fever, tuberculosis, and syphilis, and hence suggested an allergic explanation.[22] Shortly afterward Bezançon and Weil[23] independently advanced similar views. We applied methods which had proved useful in the study of the last two diseases to try to find some new etiological agent comparable to the tubercle bacillus or the Treponema pallidum. Many species of laboratory animals, including calves, were inoculated in various manners without successful reproduction of anything closely resembling rheumatic fever and without demonstration of any new etiological agent. The only microorganisms recovered with any degree of regularity from blood cultures or subcutaneous nodules were streptococci.

In the past four years, however, in collaboration with Drs. Andrewes, Derick, and Hitchcock, we have obtained experimental data with these cocci which appear to have brought some order out of what was previously a confusing situation. The detailed evidence for our work is published elsewhere.[24, 25, 26, 27, 28, 29, 30] It is sufficient to state here that by intracutaneous inoculation with certain strains of streptococci we have been able to induce in rabbits a general state of hypersensitiveness which resembles in many particulars the allergic state seen in tuberculosis and syphilis. A most important requirement for the induction of this state is the production of a focal lesion somewhere in the body. Lesions repeatedly produced at suitable intervals increase the hypersensitiveness. Once induced it can often be maintained over comparatively long periods by making a deep focus of suitably infected agar.

The tissue of a highly hypersensitive animal shows a greatly intensified response to inoculation with very small amounts of streptococci; for example, where a normal animal shows little or no reaction to 0.0001 c.c. of broth culture, the hypersensitive animal has a lesion containing 100 to 400 cubic millimeters of exudate and proliferate, and a highly sensitized animal at times shows an edematous lesion 10 to 12 mm. in diameter following inoculation of 0.000001 c.c., while a normal animal shows only a needle prick. Microscopically the lesion of a hypersensitive animal shows early a much more marked exudation than is seen in the lesion produced by the same size inoculum in a normal animal. But a point of almost as great interest is that an intravenously inoculated rabbit does not show hypersensitiveness of this type. On the contrary, with repeated intravenous immunization it shows less and less reaction to intracutaneous test inoculation; and these cutaneous lesions in an immune animal show less exudation microscopically than does a normal control. We thus have two types of tissue response to nonhemolytic streptococci developed according to the manner in which the animal is originally inoculated: hypersensitive, following inoculation into the tissues, and immune, following intravenous inoculation.

But these two states are not specific when specificity is considered from the viewpoint of cultural or serological strain specificity. While a hypersensitive animal usually reacts more strongly to the strain with which it is sensitized, it also overreacts to more distantly related strains. Likewise, an intravenously inoculated animal shows the immune type of tissue response to subsequent intracutaneous inoculation with heterologous strains. A similar observation was made by Kuczynski and Wolff,[31] who observed that intravenous immunization of mice with green streptococci markedly increased their resistance to hemolytic streptococci, and by Tillett,[32] who showed that active immunization with rough pneumococci rendered a rabbit immune to all types of pneumococci.

We have, furthermore, been able to carry some of these studies over into the clinic, and to show that most patients with rheumatic fever show much larger reactions following intracutaneous inoculations of vaccines or of nucleoproteins prepared from streptococci, and of filtrate of nonhemolytic streptococci, than do normal people. The observations of Birkhaug,[33] Kaiser,[34] Small,[35, 36,37] and Straus,[38] also indicate similar hypersensitiveness in the rheumatic fever patients they studied.

In one respect our observations differ from Birkhaug's, viz., that patients with active rheumatic fever show skin hypersensitiveness to filtrates of various types of nonhemolytic streptococci.* Mackenzie

*Birkhaug. Personal communication has confirmed our observation.

and Hanger's[39] observations indicate also that the specificity of skin reaction is not linked to any one type of streptococcus, nor in their observations was any one type of disease linked with hypersensitiveness to streptococci. While they did not give their complete data, it is interesting to note that many of their hypersensitive patients were suffering from rheumatic fever.

We[28] have furthermore observed that rheumatic fever patients usually show a late tuberculin-like febrile reaction following intravenous injection with small doses of vaccine or of nucleoprotein prepared from hemolytic streptococci. While we do not claim that rheumatic fever is the only condition in which these reactions are found, still we feel that this kind of hypersensitiveness plays an important rôle in producing the peculiar picture of the disease. Zinsser[40] on hypothetical grounds has recently advanced similar views. Indeed, we are appreciating more and more that it is the peculiarity of the tissue response rather than a history of polyarthritis that is the important factor. The recently published statistics of von Glahn[41] emphasize the frequency with which rheumatic carditis may occur in the absence of a history of polyarthritis.

In the production of most diseases a number of contributory factors must be present. As yet we are unable to state why all persons hypersensitive to streptococci do not have rheumatic carditis, any more than we can determine why all scarlet fever patients do not develop nephritis, or even why some with Streptococcus scarlatinae infections do not have a rash; only with the acquisition of much additional information can we furnish completely satisfactory answers to these questions. But the existence of a state of hypersensitiveness to streptococci can account for many of the known features of the disease. The lack of strain specificity of this state could easily make understandable the etiological rôle of the several types of streptococci that have been recovered from patients with this disease. The extensive exudative reaction seen in hypersensitive rabbits following implantation of small numbers of streptococci explains how such relatively avirulent microorganisms could produce extensive edema and marked outpouring of cells in patients who are similarly hypersensitive.

For a period following Aschoff's discovery of the submiliary nodule, which seemed to be chiefly a proliferative reaction, pathologists neglected the exudative reaction which is so evident to clinicians in the swelling seen in poylarthritis; but lately the studies of von Glahn[42] and Pappenheimer,[43] MacCallum,[44] and Fahr,[14] and our own observations[45] have directed attention to the importance of exudation as a part of the tissue reaction. If we can assume that the submiliary nodule represents mainly the proliferative response of the tissues to implantation of bacterial body or some particulate product of such

bacterial body, then it can be readily understood how such an exudative response as edema might occur at some distance and lead to distinct clinical symptoms. The disappearance of the exudation about joints following the administration of salicylates is a common experience; a similar decrease of exudation in the heart is the most plausible explanation of the recent observations of Levy and Turner[46] who demonstrated the disappearance after administration of salicylates of abnormally prolonged conduction time in several patients with rheumatic fever. The occurrence of such an exudation, which may appear and disappear with surprising rapidity, would also explain in part the frequency with which electrocardiographic evidence of cardiac involvement occurs and the numerous changes that may be demonstrated in a single patient.

In our opinion, edema of the valves may account for the localization of verrucae at the line of closure. Elsewhere[22, 47] we have called attention to the occurrence of widespread interstitial valvulitis early in the disease, in some instances before any verrucae were demonstrable. If edema in valves approximates in intensity that of joints, it is easy to understand how such an edematous structure impinging on another similar structure thousands of times a day would lead to injury to the endocardium sufficient to favor the deposition of thrombotic deposits in the form of verrucae. Coombs[48] also considers that interstitial valvulitis is the essential rheumatic valvular lesion.

But in this connection we must consider the recent work of Siegmund,[49] Dietrich,[50] and Kuczynski and Wolff.[31] Siegmund, particularly, has studied the reaction of vascular endothelium to infection and shown that this endothelium reacts quickly following intravenous inoculation with various bacteria. Small intimal "Fibrinknotchen" are formed in which the bacteria are quickly destroyed, but during the evolution and involution of these small intimal nodules various pictures are reproduced which closely resemble certain features of endocarditis. With increasing immunity there is increasing intensity of response. His findings can be readily brought into relationship with subacute bacterial endocarditis, but he did not consider the possible differences between a hypersensitive and an immune state in his animals, such as we have been able to reproduce.

Dietrich, on the other hand, suggests that increased sensitivity may account for the implantation of bacteria on the margins of the valves. He inoculated two series of rabbits intraperitoneally with staphylococci, and one series intracutaneously by rubbing broth cultures into the shaven skin. Subsequent intravenous inoculation with cultures of low virulence resulted in the formation of verrucous lesions along the valve margin in a number of instances. Unfortunately, a microscopic examination of these lesions was not given.

In all of the work of the German school the extension of the infection of the valve from the external surface inward is stressed. In this country, on the other hand, the weight of the evidence is thought to indicate that infection of the valve occurs through the vessels supplying the valve. The work of Kugel and Gross,[51] of the students of Winternitz,[52] of Kerr,[53] of Bayne-Jones[54] and others, all show that vascularization of the valves is much more extensive than was formerly known. Both Gross and Winternitz have found that endocarditis and vascularization of the mitral valve run hand in hand, and feel that all of the evidence points to such vascularization as being primary. It is interesting to note that endocarditis occurs most frequently in rheumatic fever of children at an age when vessels are most numerous, and that liability to endocardial involvement decreases with age in about the same ratio as vessels are known to disappear; also that frequency of involvement of the respective valves is in direct ratio to demonstrated frequency of vascularization. It is a general rule that localization of rheumatic fever lesions occurs most readily in dense connective tissue where there is constant motion. The valves represent such a tissue. If hypersensitiveness to streptococci of the vascular and perivascular tissue of the valves of a rheumatic fever subject is at all comparable to that of his subcutaneous tissues, or to that of the hypersensitive rabbit, it is readily understandable how interstitial valvulitis might arise from implantation of streptococci or their products in these vessels when the individual is hypersensitive. Indeed, we have observed distinct endo- and perivascular reactions in small blood vessels in the valves comparable to similar lesions in the synovial and perivascular tissue removed by biopsy from the knee joint of patients with active rheumatic fever.

The reaction in the vessel wall may indeed play a larger part in the production of other cardiac disturbances than we have heretofore considered probable. Fahr[14] called attention to the frequency of some form of vascular lesion in the majority of 32 cases of rheumatic carditis which he examined, and suggested that these lesions would account for areas of transient or partial anemia in the heart wall which in turn would explain the muscular weakness which is often so prominent a clinical feature. He goes even farther and suggests that similar vascular alterations may account for some cases of malignant sclerosis. Von Glahn and Pappenheimer[55, 56] have still more recently directed attention to the widespread distribution of vascular lesions in rheumatic fever; and Kugel and Epstein[57] have just contributed similar valuable additional evidence. Winternitz and his students[52] are actively studying the effect of lesions of the vasa vasorum and pointing out the importance of these lesions in disease of the larger arteries and veins in infection. When all of the work at present in progress is correlated, we may find that the so-called rheumatic fever reaction has

a wider import than we even now think probable. Indeed, the conception of rheumatic fever as a joint disease is becoming less and less prominent as its rôle in contributing to disease of visceral blood vessels becomes more evident.

SUBACUTE BACTERIAL ENDOCARDITIS

It is desirable next to discuss the disease known as streptococcal subacute bacterial endocarditis or endocarditis lenta from the standpoint of recent investigations. Both Small[35] and Birkhaug[33] have recently directed attention to the frequency with which rabbits develop a disease somewhat similar to subacute bacterial endocarditis when inoculated intravenously with indifferent streptococci, and we have confirmed these observations. Rosenow[58] obtained similar lesions by injecting green streptococci. But in human pathology this bacterial endocarditis is practically always secondary; in other words, the bacteria are implanted on or in an abnormal valve, and in the majority of instances the valve has been the site of an old rheumatic endocarditis.

Another interesting observation originally made by Kinsella[59] and myself, and confirmed by Libman,[60] is that all of these patients show a fairly high agglutinin titer in their serum against the streptococcus which is producing their disease. Kinsella[61] was unable to produce endocarditis regularly on the traumatized valves of dogs' hearts unless he previously partially immunized the animals. Wright[62] was able to produce bacterial endocarditis more regularly in rabbits if they were previously immunized. Wadsworth[63] has directed attention to the frequency with which horses highly immune to pneumococci develop endocarditis resembling subacute bacterial endocarditis in man. White[64] has recently observed a similar condition in streptococcus immune horses. Serum immunity and this type of endocarditis seem then to go hand in hand. We have never found a similar high degree of serum immunity in rheumatic fever patients against the strains of streptococci occasionally recovered from them. This, moreover, corresponds with our findings in hypersensitive rabbits, where agglutinins and precipitins against the sensitizing streptococcus are never very strong. Small[35, 36] and Clawson[65] both report the finding of weak agglutinins against the streptococci which they recovered from patients with rheumatic fever, but here again, let us emphasize, the titer was low. In this connection another observation made by Howells and Corrigan[66] is of much interest. These authors found that none of seven patients with subacute bacterial endocarditis showed skin reactions to filtrates of streptococci, and we have confirmed these findings in two instances. Kinsella and Garcia[67] also were unable to induce any local reaction by inoculating a patient suffering from subacute bacterial endocarditis with living streptococci, or by making an agar focus inoculated with these streptococci. This is

directly in line with our observations that intravenously immunized rabbits show less intense reactions than do normal animals to cutaneous inoculation with streptococci or with filtrates. What more do we find clinically? Practically none of the embolic phenomena of subacute bacterial endocarditis are accompanied by extensive exudation, but the evidence of tissue injury is closely confined to the area of the embolus. We have never seen marked edema about a painful joint in the neighborhood of Osler's nodules, nor about a vessel in the lobe of the ear where we could observe the relationship of the embolus to the blood vessel. We have recently observed a patient with this type of endocarditis involving chiefly the right heart, but in spite of numerous pulmonary emboli no pleural effusion occurred. Another patient recently under our care entered the hospital with rheumatic fever and during the next two months had all of the exudative phenomena usually seen with pericarditis, pleurisy, and polyarthritis. He then seemed to recover, but after an acute sinusitis developed classical signs of subacute bacterial endocarditis, and showed Streptococcus viridans repeatedly in blood cultures. His blood which had been saved from the period when he was suffering from polyarthritis showed no agglutinins, while that obtained after the development of subacute bacterial endocarditis showed them in a fairly high titer. No exudative phenomena were observed during this latter period.

The interesting observations of Rothschild, Sachs and Libman[68] may also be added to the evidence concerning the relationship of this disease and rheumatic fever. In 61 cases of bacterial endocarditis examined by graphic methods they found abnormal increase of the conduction time only ten times and changes in the QRST complex of the electrocardiogram only four times. This, compared with lengthened P-R interval in 23 out of 65 cases of rheumatic fever and alterations in the QRST complex in 52 cases, and with similar findings by us,[69] shows that instrumental signs of extensive parenchymatous irritation of the heart are as rare in subacute bacterial endocarditis as are peripheral signs of exudation.

From all of this evidence we may conclude that, in general, subacute bacterial endocarditis is accompanied by a state of relative tissue immunity, and that the presence of antibodies in the serum under experimental conditions is a concomitant phenomenon in the course of this disease. We then have the apparent paradox of an active and usually fatal infection in a biologically immune individual. How the microorganisms originally colonize in or on the valve is a mystery. One possible explanation suggests itself: the streptococci in the blood stream of an immune individual may be agglutinated in masses of sufficient size so that when caught in a tissue, such as that of the heart valve, in which the natural factors for resistance are but slowly mobilized, they are large enough to start the growth of a colony; and

this colony deep in the tissues soon increases sufficiently to remove many of its members from the influence of either tissue or circulating phagocytes. The blood of these patients is highly bactericidal to the infecting organisms; hence the only possible explanation for the continuation of the disease is that the bacteria are in a situation where this bactericidal action cannot be exerted. If this explanation is correct, the failure to effect a cure by attempting actively or passively to increase the immunity of patients suffering from this disease is understandable. All of the conditions for effective general immunization are present in such a patient. The etiological agent is being constantly supplied to the tissues with a consequent immune response. In rare instances this response is doubtless effective, but in most patients the streptococci are situated so that no immunity either active or passive can be made sufficiently intense to destroy them. Chemotherapeutic measures have been equally ineffective, and probably for similar reasons; the mechanical factors inherent in the growth of the streptococci on or in the heart valves are such that no bactericidal agent can be effectively applied.

The opinion was expressed several years ago by Lewis and Grant,[70] and by Libman[71] that nonhemolytic streptococci probably circulate occasionally in the blood stream of most individuals. The recent observations of Kugel and Epstein[72] substantiate this opinion. The important factor in the production of disease rests not alone in the presence of microorganisms in the blood stream, but in the ability of that particular microorganism to elaborate substances which can set up certain types of tissue reaction, and also in the capacity of the tissues to respond in a particular manner to these substances. In the differences in the response of the tissues we see a possible explanation between the normal person, the man sick with rheumatic fever, and the individual with subacute bacterial endocarditis.

SYPHILIS

A brief discussion of syphilitic heart disease is required not only because of the importance of the rôle of the Treponema pallidum in the production of cardiac disorders, but also because the disease represents a condition where allergy has been shown to play a prominent part in the pathological changes encountered during the course of the infection. It has been demonstrated that without the development of such an allergic state the spirochetes may be tolerated by the body without exerting a harmful effect.[73] They can lie dormant in tissues without these tissues showing any evidence of their presence until the general reactivity of the body is altered; then cellular changes in their neighhood make evident the effort of the body to rid itself of these foreign invaders. There are also periods of relative immunity in contrast to hypersensitiveness on the part of the tissues, as is indicated by the

work of Chesney and Kemp,[74] Nichols[75] and others. But with the passage of years there develops an increasing degree of hypersensitiveness so that in an individual where early the general evidence of the reaction of the tissues is only a superficial macule or maculopapule, later the response is many times as intensive in the form of a nodule or gumma. I do not mean to imply that the late reactions always take the form of gummas, but rather that these lesions represent a relatively intense form of tissue response to the presence of spirochetes. This disease also represents, par excellence, the importance of the rôle of lesions of the blood vessels in inducing alterations in the tissues supplied by them.

An appreciation of the nature of the evolution of syphilis is necessary if we are to find any reasonable explanation of the peculiarity of the cardiac symptoms. Although Brooks[76] and others have directed attention to the frequency with which evidence of cardiac involvement may occur early in the disease, it is clear from statistical studies, such as those made by Wyckoff and Lingg[77] as well as from the experience of clinicians and pathologists for decades, that the baneful effects of syphilis on the heart and aorta are not made very evident until years after the initial lesion. The occurrence of spirochetes in the blood early in the disease has been repeatedly demonstrated; hence we must conclude that the heart is exposed to them as much as are the other organs. But it is only after the passage of years accompanied by an ever-increasing degree of hypersensitiveness that the intensity of cardiac tissue response is sufficient to make a marked impairment of myocardial function clinically evident. There can be little doubt that during this period of so-called latency there may have been slowly progressing injury of the muscle; often lesions of the aorta and aortic valve have resulted in a compensatory hypertrophy of the myocardium, but it is only when this compensation fails or when progressive injury to the muscle fibers reaches a certain degree, or when lesions of the cardiac blood vessels are extensive enough to interfere seriously with an efficient blood supply to the heart muscle, that this muscle fails to work effectively. Warthin[78] has clearly shown how few spirochetes may be demonstrable in the sites of diffuse interstitial myocardial lesions, and that such lesions are not necessarily in the form of gummas. It is possible that just as gummas represent the most perfectly developed and typical form of marked allergic tissue response to Treponema pallidum, so the Aschoff body may only represent a typical reaction to the causative agent of rheumatic fever. In both diseases there are diffuse types of inflammatory reaction and in both involvement of the blood vessels plays an important rôle in compromising the nutrition of the heart. In the manner in which the aorta and the aortic valves are involved the two diseases further resemble one another. A great difference in the two, however, is the rapidity and

intensity with which involvement may take place in rheumatic fever and the slowness with which it does occur in syphilis; nevertheless, chronicity and periods of activity alternating with intervals of apparent latency are often encountered in both maladies.

SEPTICOPYEMIA

The importance of septicopyemic involvement of the endocardium consists in the ease with which infective emboli are constantly swept into the blood stream and thus become carriers of the bacteria to other parts of the body. There is also the additional picture of severe intoxication and cachexia which is quickly reflected in a weakening of the poisoned heart muscle. These are both more deleterious factors in determining the outcome of the disease than is the ulceration of the valvular tissue resulting from the growth of the bacteria in the endocardium. In most instances a fatal issue occurs before the mechanical factor of inefficient heart valve, per se, can make itself felt.

TOXIC MANIFESTATIONS

It is often difficult to determine just how great an influence a mild poisoning of the myocardium is exerting in the abnormal action of the heart encountered in most infectious diseases. The experiments of Newburgh and Porter[79] indicate that the heart may develop a type of resistance to the poisoning that results in Friedländer bacillus pneumonia, for when blood from infected animals was supplied to a normal animal's heart, it quickly showed evidence of poisoning, whereas an infected dog's heart tolerated such blood much better. Levy[80] demonstrated that in patients with lobar pneumonia there was usually roentgenographic evidence of cardiac dilatation of from 10 to 30 per cent. Whether this is a direct result of toxic action of some hypothetical poison on the myocardium, or a response of the heart to extra demands resulting from the general infection, or a combination of both factors, is a question not as yet decided. That such hearts will show the usual response to such cardiac tonics as digitalis was clearly demonstrated by the work of Cohn and Jamieson.[81] Indeed, it may be stated as a general proposition that when in any infection, be it general or cardiac, the heart muscle and conduction system are too badly damaged to respond to digitalis, the patient is, indeed, in a precarious condition.

CONCLUSION

As indicated early in this communication, no attempt has been made to cover completely all of the problems presented by the heart in infection. Indeed, to try to do this would prove futile, for the subject is one that could not be covered in its entirety in a large volume. An effort has been made rather to draw an outline in which certain well-

recognized types of response of the respective cardiac tissues would provide a satisfactory explanation for the various features of heart disease in so far as active infection is concerned. I do not wish to leave the impression that any single type of cardiac infection includes only one type of tissue change; indeed, such is far from the case. The tissues in general have only a few ways in which they can respond to injury; the peculiar picture in any specific disease is determined by the relative amount of response of one or another type and also by the manner in which the special functions of any given organ or tissue are influenced by the particular structural changes.

In some instances an explanation of the nature of the structural changes is based on theories well substantiated by clinical and experimental evidence; in other instances on theories in the process of evolution. All that one can hope to accomplish in the way of a general description of such a complicated subject is to present a picture in which the various phenomena are correlated in a manner most in accordance with current knowledge and belief. With these reservations in mind we may conclude with a review of the type lesions of the heart in infection as being first toxic, as in diphtheria and early in scarlet fever; second allergic, hyperergic or hypersensitive, as late in scarlet fever, in rheumatic fever and in syphilis; third, bacteremic and biologically immune, as in subacute bacterial endocarditis; and fourth, bacteremic, toxic and cachectic, as in acute septicopyemia.

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THE SURGICAL TREATMENT OF ANGINA PECTORIS

What It Is and What It Should Be

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THROUGHOUT the world numerous papers have been published concerning the surgical treatment of angina pectoris. These articles reveal the great interest in this new method of treatment which has developed among those physicians who wish to procure for their patients, suffering from this terrible disease, greater improvement than medical treatment alone can ordinarily provide.

Since in the beginning only papers most favorable to the surgical treatment of angina pectoris were published, several cardiologists† and surgeons have in the last few years found it necessary to warn their confrères against a method which seemed to them both dangerous and useless. If one is at all skeptical, one might think that this method of treatment is experiencing the same evolution as is seen periodically with many other new ideas; viz., initial growth, then adoption with enthusiasm by a few, and finally disappearance after a few years' fashion, leaving behind no other traces than a bulky literature which is rapidly forgotten. Convinced that the surgical treatment of angina pectoris merits a better destiny, we present this paper.

We feel that this particular procedure is both desirable and justifiable, and, as proof of our statement, we quote an actual case rather than giving a theoretical explanation.

Rü . . . Albert‡ was sent to Professor Leriche in 1925 by a physician in a small town in Alsace. The patient, who was fifty-one years of age, had never been seriously ill; he had never had any venereal disease, and his blood Wassermann was negative. For several years he had complained of crises of precordial pain which were severe and accompanied by anguish and a sensation of retrosternal constriction. The crises came once in six or eight weeks. They began, usually, in the evening after dinner with a pain which began behind the left shoulder, radiating anteriorly in the left hemithorax but never going down the arm. The crises lasted about ten minutes and terminated with a very marked flood of tears. For several days after an attack the patient felt tired.

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†We do not ignore the fact that the great English cardiologist, Mackenzie, never recognized the surgical treatment of angina pectoris. He, however, had had no personal experience with this form of treatment and based his opinion on theories which we cannot consider here.

‡We shall give here only a brief résumé of this case. The complete history has been published in the thesis of one of us (see Fontaine[12]). This observation together with those of three other cases of angina pectoris will also be found in our paper[21] published in 1927.

The physical examination was completely negative. The blood pressure was 150/90 mm. Hg.; the electrocardiogram was normal, but the x-ray showed a slightly enlarged left ventricle and aortic arch.

The diagnosis of angina pectoris was confirmed by competent medical specialists, and after a period of observation the patient was operated upon on the twenty-fifth of February.

Under local anesthesia we extirpated the superior cervical ganglion and the cervical trunk down to the stellate ganglion. The rami communicantes of this were cut and the nervus vertebralis was interrupted. The patient recovered without any complications, but two weeks following the operation presented a typical crisis of angina pectoris. This was the last. Never since then has he had the remotest symptom, and his recovery now dates back two and a half years. During this period he was regularly followed; we saw him at least once every two months. At the last examination his general status was perfect and the disappearance of the angina pectoris remained complete. The heart was clinically normal, the electrocardiogram showed nothing pathological and the x-ray findings were the same as before the operation.

During this period he was presented several times at medical societies where he was examined by competent physicians all of whom were astonished at the excellence of the results obtained. In July, 1925, the members of the Society of Clinical Surgery saw him during their visit in our clinic at Strasbourg. Two years later, in March, 1927, a still greater number of surgeons, visiting from London, were convinced that the results remained unchanged.

Objections might be made on the ground that this case was a very good risk, since the crises were rare and the heart was in good condition. We would not contradict this, but this man had had before the operation, in spite of rigid medical treatment, a crisis of angina pectoris severe enough to interfere with his work. In less than a month following the sympathectomy he returned to work at which he has since continued without interruption.

This case was not the only one with which we attained success; incidentally, many other surgeons have obtained equally satisfactory results. We chose this as a typical case to demonstrate what we feel it is possible to do by the surgical treatment of angina pectoris.

In 1925 we made a study[12] of the reports of one hundred cases which had been operated upon; ninety-four of these furnished the material for the following statistics:

1. Disappearance of the crises in 59 cases, 62.7 per cent.
   Of these 59 cases there was
   - Relief for more than 3 months in 29 cases (30.8 per cent).
   - Relief for less than 3 months in 17 cases (18.1 per cent).
   - Relief for an unknown period in 13 cases (13.8 per cent).
2. Temporary disappearance of the crises in 3 cases, 3.2 per cent.
3. Marked improvement in 6 cases, 6.4 per cent.
4. Slight improvement in 2 cases, 2.2 per cent.
5. Failure in 6 cases, 6.4 per cent.
6. Unknown results in 5 cases, 5.3 per cent.
7. Operative mortality (due to operation and not to progress of the disease) in 13 cases, 13.8 per cent.

One year later Dr. Cutler[7] published the following statistics covering one hundred and twenty cases:

1. Good results in 47 cases, 40.0 per cent.
2. Improvement in 52 cases, 43.3 per cent.
3. No improvement in 10 cases, 8.3 per cent.
4. Unknown result in 3 cases, 2.5 per cent.
5. Operative mortality (death within twenty-four hours) in 7 cases, 5.8 per cent.

Diaz Sarasola[31] recently collected one hundred and thirty-six cases; fifty-two of which he utilized in the following figures:

1. Clinical healing in 16 cases, 30.7 per cent.
2. Clinical improvement in 16 cases, 30.7 per cent.
3. No result in 7 cases, 13.4 per cent.
4. Operative mortality in 13 cases, 25.0 per cent.

Since our publication in 1925, we have continued to collect data dealing with cases of angina pectoris which have been operated upon. We have collected in all about two hundred cases from the literature, but we fail to see any advantage in preparing new statistics, since so few observations have been published in sufficient detail to permit one to form a very definite opinion regarding the diagnosis, intervention and result obtained. Reports of the last-mentioned have only too often been published after an insufficient time of postoperative observation has elapsed. Taking all of this into consideration, we shall content ourselves with saying that, were new statistics prepared, they would not be essentially different from our first. These figures have only a limited value, at the best, as they merely substantiate our opinion that the surgical treatment of angina pectoris can give complete relief and, when it falls short of that, produces a very marked improvement which is greatly appreciated by the patients. The unsatisfactory results and failures together number less than 20 per cent.

Instead of discussing further figures which are the result of imperfect statistics, as the material from which they were gathered is uncertain and inaccurate, we shall approach the question from another angle. We feel that the practical results obtained justify the present method of treatment.

The possibility of a surgical cure having been established, we shall endeavor to find out why the same results are not obtained in all cases; in other words we shall consider the reasons for failure and the methods whereby one may hope to avoid them. An analysis of all the cases of angina pectoris which have been operated upon gives us the impression that a great number of failures can be explained by one of the following: (a) insufficient or erroneous diagnosis; (b) wrong type or incorrectly executed operation. We shall consider these as follows:

THE DIAGNOSIS OF ANGINA PECTORIS AND ITS VARIETIES IN RELATION TO FAILURES IN SURGICAL TREATMENT

Correct diagnosis is frequently difficult as this disease does not always have the same clinical findings. Sometimes it is in relation to cardiac disease, forming one of its most dangerous complications; again, it is independent of all cardiac disorder. The first is referred to as organic (Gallavardin) or primary (Mackenzie) angina pectoris; the second, as inorganic, secondary or neurotic. In considering surgical treatment, this differentiation should always be made. It is always necessary to know, too, that secondary forms of angina pectoris are frequently due to long distant reflexes from other organs, e.g., the abdominal. It would certainly be unwise to submit to a cervical sympathectomy a patient whose anginal crises are due to an excessive use of tobacco or relative to disease of the bladder. These facts are well known and yet if one reads the papers concerning angina pectoris one sees that many surgeons were satisfied to find "typical crises of angina pectoris" and did not try to discern their origin. Before operating upon a patient it is absolutely necessary to make a very complete examination in order not to overlook an irritative point, the removal of which would be sufficient to relieve the crises.

We shall consider here, however, the primary and omit the secondary form. In the former the differential diagnosis between angina pectoris and cardiac asthma is usually simple. Nevertheless, one finds in the literature real cases of cardiac asthma which have been operated upon under the diagnosis of angina pectoris. Considering facts such as these, Levine and Newton[23] stated that while no one would have the audacity to say that, because antidiphtheritic serum did not cure a case of Vincent's angina it was useless, several authors have been quite ready to declare that the surgical treatment of angina pectoris was a failure after they have treated several cases which were not true angina pectoris.

Real difficulties in the diagnosis of angina pectoris are encountered when one tries to distinguish it from the aortalgias and the painful precordial crises due to coronary thrombosis. The distinction between these three painful syndromes is very difficult, and we do not know whether it is always possible. The recent progress made in electrocardiography by Pardee[28] in America and by Clerc[4] in France now allows us to make a definite diagnosis of coronary thrombosis, but the distinction which Levine and Newton make between typical angina pectoris and pseudo-angina pectoris due to coronary thrombosis seems to us to be too artificial and schematic. These authors feel that a typical crisis of angina pectoris should be relieved by nitroglycerin and is accompanied by a momentary increase of the blood pressure without any modification in the rhythm and frequency of the heartbeat, while the attack of precordial pain due to coronary thrombosis

is of longer duration, should not be relieved by nitroglycerin and is accompanied by a drop in the blood pressure and increase in the pulse rate.

According to Levine and Newton such attacks are not true angina pectoris and should be excluded from this classification. This seems unnecessary if one clearly understands the true significance of the names. Angina pectoris is essentially characterized by a precordial pain accompanied by angor and the familiar irradiations. If such be true, angina pectoris is a syndrome and like all syndromes may have multiple origins. Precordial pain, whether arising in the myocardium, the aorta, coronary vessels or elsewhere, will have certain common characteristics. It would be quite simple to agree to use the term *angina pectoris* to designate only that type of precordial pain which has no relation to coronary thrombosis or aortic disease with the possible exception of suprasigmoidal aortitis. Such being the case, *angina pectoris* would occupy the same place in the group of *precordial pains* as *Biermer's disease* does in the group of *anemias*. It would be a clinical entity of unknown origin.

Personally we would prefer to give the name angina pectoris to all painful precordial crises, having the characteristics with which we are familiar in a more or less typical form, thus making angina pectoris a common factor in many cardiac diseases. Under such conditions the application of the term *angina pectoris* should be the same as that of *anemia* in relation to certain blood diseases; that is, we consider it as a syndrome in the same sense as we regard anemia as a common syndrome in these blood disorders. Such being the case, the diagnosis, angina pectoris, should never be made without an attempt to verify its etiological indication. One would not speak of anemia without giving an explanation of its origin.

In the surgical treatment of this disease it is logical to believe that, because of the possibility of multiple origin, this method will not only fail to be universally beneficial in all types of cases but that also it may not be indicated in all periods of the disease. In this connection, it might be well to consider for a moment which cases we feel are fit subjects for operation. We have tried repeatedly to answer this question by reviewing cases and, to simplify our reports, we have introduced a formula which considers all etiological and clinical factors which may enter into the picture.

Up to the present time from the two hundred cases which we have collected we have been able to compile only thirty-five complete cases which answer all the demands of Formula I. The remainder were lacking in necessary details. This number we felt was too small to justify our arriving at a definite conclusion. We did feel, however, in agreement with Levine and Newton, that all cases of coronary thrombosis with rapid evolution should be excluded from surgical treatment.

FORMULA I (DIAGNOSIS)

1. Age and sex of patient.
2. Previous diseases (especially infections, such as acute rheumatic fever).
3. Habits—alcohol, tobacco.
4. Venereal disease—Wassermann report.
5. Organic disease present—if so, what.
6. Characteristics of the crises.
   a. Period of time during which patient has had disease.
   b. Presence of previous cardiac disease.
   c. Frequency of crises.
   d. Duration of crises.
   e. Description of a crisis.
      1. Onset—by effort or decubitus, influence of meals, by day or night.
      2. Localization of pain.
      3. Localization of hyperesthesia.
      4. Other symptoms—angor, fear of impending death, retrosternal constriction.
   f. Presence of dyspnea.
7. Modifications of the heart during an attack.
   a. Blood pressure.
   b. Pulse.
   c. Rhythm.
   d. Vasomotor signs.
8. Effects of drugs upon a crisis.
9. Termination of a crisis.
10. Status of the heart between crises.
    a. Frequency and rhythms.
    b. Volume and form of the heart.
    c. Character of the sounds.
    d. Blood pressure.
    e. Electrocardiograph findings.
    f. X-ray result.
    g. Functional tests of the heart.
    h. General condition.
    i. Presence of symptoms of cardiac decompensation.
11. Precise clinical diagnosis.
    a. The heart.
    b. The aorta.

The best results appear to be obtained in those cases where the attacks are rare, as for example, the one cited as an illustration at the beginning of this paper. For this reason we feel that no one is justified in requiring a long period of medical treatment before undertaking the surgical procedure. In the early stages of the disease cervical sympathectomy is a very benign operation, and our experience leads us to believe that medical treatment is of little benefit. We should like to urge the point that in this procedure, as in all others, there is one time when surgery is indicated and another when it is too late and the opportunity of obtaining a good result has passed.

Correct diagnosis is an exceedingly important factor, but this does not lessen the necessity of a correctly executed operation, and this introduces our next point.

THE NECESSITY FOR A CORRECTLY CHOSEN AND PROPERLY EXECUTED OPERATION IN THE SURGICAL TREATMENT OF ANGINA PECTORIS

Every surgeon who contemplates surgical interference in a case of angina pectoris should have definitely fixed in his mind the result which he hopes to obtain. His purpose is not to cure the patient by suppressing the cause of the disease but rather to make the attacks impossible by interrupting the mechanism. Bearing this in mind, certain arguments—for example those stated by Ormos[27] in his recent paper, which try to justify the surgical treatment by the existence of histological modifications in the cervical sympathetic ganglia—seem dangerous to us. They encourage the surgeon to treat the cervical sympathetic system in angina pectoris as he would an organ with a malignant tumor, in which case he tries to resect as much as possible in an effort to destroy the lesion. It is true that histological lesions are sometimes found in the ganglia in the form of scleroses, inflammatory cell reactions or cellular degenerations, but these are inconstant and have no specific value. They are found in many other conditions and are very difficult to distinguish from the purely involutive ganglionary lesions which normally occur during life. In any event, it seems certain that such histological changes are secondary and play no rôle in the clinical picture.[22, 30]

In other words, a cervical sympathectomy performed in this particular condition is not an etiological treatment. We only interrupt the path of the reflexes which give rise to the crisis. If one fully comprehends this statement, one must consider the operation as a strictly neurosurgical procedure which demands the greatest precision.

Why then have several writers forgotten this principle when they have published the results of cases of angina pectoris treated by the resection of a nerve "having the direction and route of the cervical sympathetic but possessing no ganglia"? These same men would certainly criticize very severely reports of the treatment of *tic douloureux de la face* by the resection of a nerve having only "the direction and route of the trigeminal." It is interesting to note that one surgeon condemned the surgical treatment of angina pectoris after he had performed one bilateral operation in which he was unable to decide whether it was the sympathetic, the vagus, or the recurrent which he cut. Such cases are unworthy of consideration.

One may feel that such precision as we demand is unnecessary, considering the fact that very different methods have produced practically the same results. If the simple section of the depressor nerve will produce the same therapeutic effect as the extirpation of the entire cervicothoracic sympathetic, the natural conclusion is that it is sufficient to perform any sort of operation upon the cervical sympathetic or parasympathetic in order to obtain a satisfactory result. Such conclusions cannot be proved and we doubt that all operations

really do produce the same result. The fact that some authors have published statistics favorable to partial sympathectomy, while others, basing their conclusions upon exactly the same material, advise cervicothoracic extirpation, would indicate only that the material used was poor and that the cases might be interpreted differently. The following example may illustrate this point:

Last year Professor Antonelli[1] presented before the Royal Académie in Rome a very carefully studied case of angina pectoris which had been operated upon during a period of cardiac decompensation. The patient recovered, the angina pectoris disappeared, and the heart became regular once more.

This particular case was presented as the first to be done in Italy by the integral *Jonnesco method*. This includes the resection of the stellate ganglion. Ferretti, who performed the operation, says in his operative protocol that he extirpated the superior ganglion through an incision behind the sternocleidomastoid, then followed the cervical sympathetic trunk below and saw the middle cervical ganglion which was very small. Following that he discovered the stellate ganglion in front of the inferior thyroid artery and removed it!

No anatomist has ever reported such an anatomical construction. We do not believe that there is a stellate ganglion in front of the thyroid artery. The true stellate is always deeply buried in the thorax behind the vertebral artery (Fig. 1); thus we are inclined to think that in this case the stellate was not resected and that the ganglion removed was either a duplicated middle or large intermediate ganglion.

This being true, why should such cases be reported in an effort to justify complete cervicothoracic operations as opposed to the conservation of the stellate ganglion? They only tend to make more confusing a question which needs more light thrown upon it.

Cervical sympathectomies are delicate operations, especially when performed in the region of the stellate ganglion, and even having followed a good technic, it is difficult to be certain that we have accomplished all that we desired. A recent case of Dr. Aubert's,[2*] demonstrates this. He performed an inferior cervical ramisection following the principles advocated by us in the *Gazette des Hôpitaux*.[20] The operation done under local anesthesia proved very simple. He succeeded in identifying the prethyroidal sympathetic and the vertebral artery, which he retracted, without any difficulty. Behind this artery he discovered the stellate ganglion and cut the rami com-

*We have not offered this observation as a criticism of the technic of Dr. Aubert. This mistake, we think, is probably very frequent and we cite this instance merely to show how difficult it is to be sure that everything is correctly done. Only one point might have warned Dr. Aubert that this was not the stellate ganglion, and that was that he found the ganglion behind but exterior to the vessel and the real stellate is behind and always interior to the vertebral artery.

municantes. Aubert completed his operation convinced that he had accomplished what he considered necessary and that he had done a fine piece of dissection.

Unfortunately his patient died the following day. In the autopsy he found that only the rami communicantes of the intermediate ganglion had been cut and that those of the stellate remained intact.

If this patient had not died and his symptoms had not been relieved by operation, the procedure known as the *method of Leriche* would have been condemned rather than the ability of the surgeon to apply it. This all shows that it is difficult to be sure that our work is as complete as we at the time think.

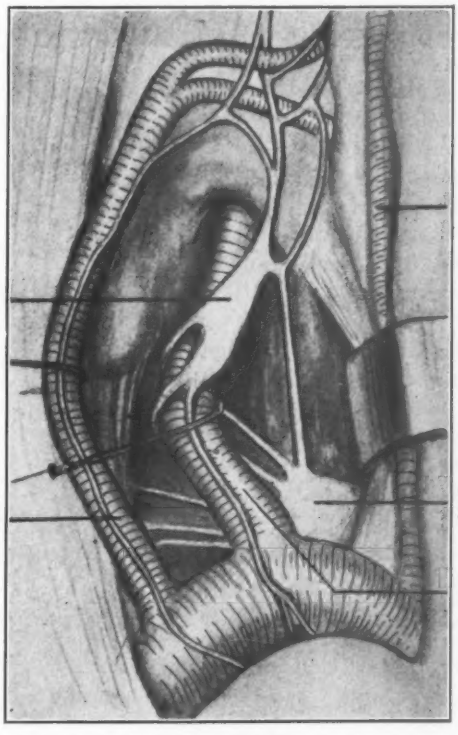

Fig. 1.—Schematic drawing showing the position of the stellate ganglion behind the vertebral artery.

Taking all such conditions into consideration, exactly what definite procedure should one follow in the surgical treatment of angina pectoris? The absence of sufficient detail in the cases operated upon and the fact that the majority have been followed for an insufficient length of time make it impossible to answer this question. One must wait until there is a greater experience to draw from before arriving at a definite conclusion as to what is the most effectual and least dangerous method. Meanwhile, it would be well to keep accurate records of all cases available considering not only the subjective improvement of the patient but the functional modifications of the heart

and certain other factors of interest. With this object in view, we have originated the following form:

FORMULA II (THE OPERATIVE AND POSTOPERATIVE EVOLUTION)

1. Name and age of patient.
2. Precise diagnosis.
3. Operation performed.
   a. Anesthesia.
   b. Side operated upon.
   c. Incision made.
   d. Actual procedure.
   e. If more than one operation, an accurate report of each.
4. Final results.
   a. Length of follow-up period.
   b. Result obtained.
      1. Definite disappearance of crises.
         a. Without persistence of any symptoms.
         b. With persistence of slight symptoms—angor, irradiation of pain, etc.
      2. Temporary disappearance of crises, period of time.
      3. Improvement in the following:
         a. Diminution of the frequency of the crises.
         b. Diminution of the intensity of the crises.
         c. Improvement of the cardiac function.
      4. Very slight improvement.
      5. Failure or aggravation—if the latter, which symptoms became worse.
      6. Death.
         a. Length of time after operation.
         b. Operative or nonoperative death.
         c. Circumstances.
         d. Post-mortem results.
5. In multiple operations:
   a. Status between operations.
   b. Time between operations.
   c. Reasons for operation—whether systematically several times or failure of the first intervention.
6. Functional status of the heart after operation.
   a. Modifications of rhythm and pulse.
   b. Modifications of blood pressure.
7. Postoperative complications due to the sympathectomy.
   a. Localized pain.
   b. Cephalalgia.
   c. Sensory disturbances (hyper- or hypoesthesia).
   d. Muscular atrophy.
   e. Laryngeal and pharyngeal complications.
8. Case classification.

In this latter connection, it would be well if surgeons would accustom themselves to the use of a more uniform nomenclature. We frequently find in medical literature observations where, in spite of the etymology of the words, the term *cervical sympathectomy* is used for the simple section of the cervical trunk, while again the same surgeons will very modestly call *sympathicotomy* the removal of the entire cervicothoracic trunk.

The following outline gives the terminology which we usually use. In classifying the results obtained we consider:

1. Excellent results; these are cases with a complete disappearance of all symptoms or disappearance of the crises and persistence of very slight symptoms.
2. Good results; these include great improvement and the temporary disappearance of the crises if the relief lasts a minimum period of three months.
3. Unsatisfactory results; these cover all cases in which there is only slight improvement, failure or in which the disappearance of the crises is very temporary.
4. Aggravation.
5. Mortality; this should be carefully distinguished from death due to the evolution of the primary disease.

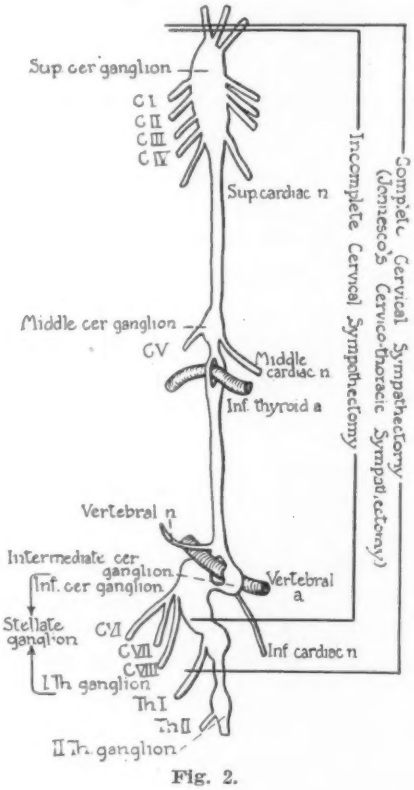

Fig. 2.

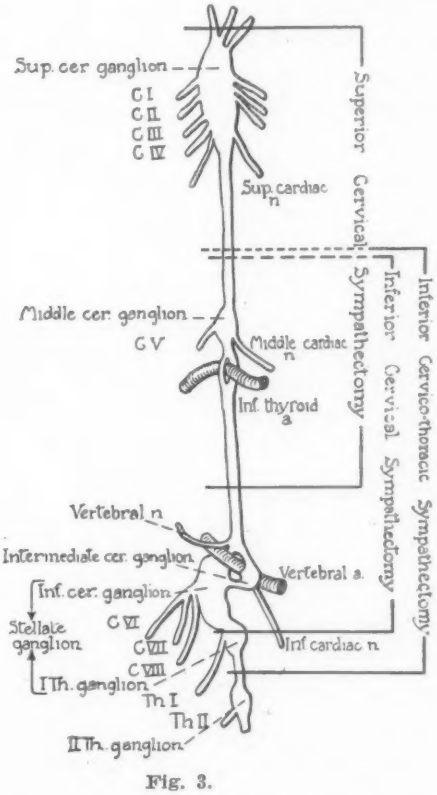

Fig. 3.

This leaves no classification for unknown or uncertain results, as we feel these should be discarded as useless; they only make the statistics less clear.

Up to the present time, our number of complete cases fulfilling all the demands of our formulas does not justify our making a definite statement recommending any special procedure as the best operation, but we do feel that some are better than others and in this connection would consider the following: the choice of a rational operative procedure in the treatment of angina pectoris (Figs. 2, 3, and 4).

Any surgical treatment of angina pectoris is performed with the idea of improving the patient's condition by interrupting the reflex

path of the anginal crises. Such an interruption is theoretically possible in two places—on the ascending or the descending way of the reflex. When François Frank[13] conceived this idea, he considered the section of the ascending fibers. The same idea predominated in Jonnesco's mind when, years later, he undertook to put Frank's ideas into actual practice, and it has since been followed by those who have been Jonnesco's disciples. He recommended the interruption of the ascending path by extirpating the entire cervicothoracic trunk. Such a procedure cuts many more nerve fibers than is necessary for the surgical relief of angina pectoris. Having observed this, Daniélopolu

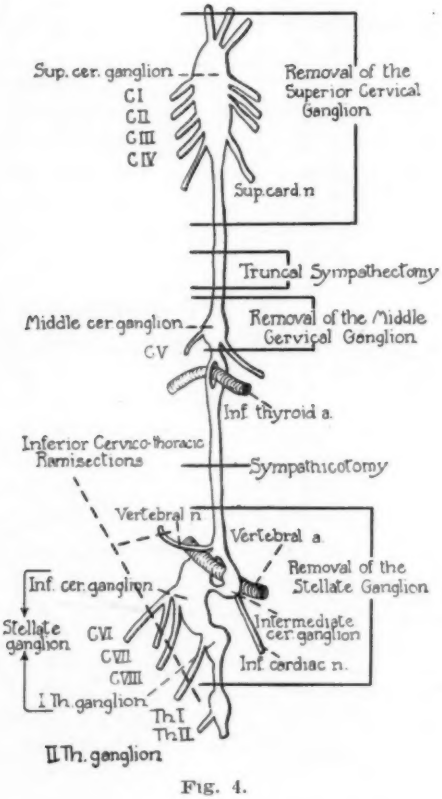

Fig. 4.

called attention to the fact that since only section of the sensory fibers was desired, it might be of interest to save the motor fibers, as their integrity might be of value in the proper functioning of the heart.

The reader is, doubtless, familiar with the effect of Daniélopolu's[8] criticism upon Jonnesco's technic—endless discussion and a lengthy dispute. In defense of his method Jonnesco[18] stated that this operation should always be done, as the purpose of the surgical treatment was not to cut the sensory fibers of the sympathetic, as first advocated by Frank and himself, but rather to resect the motor fibers of the heart. Goldschneider[16] and several others have agreed with this point of view.

The cases of angina pectoris treated only by resection of the superior cervical ganglion seem to confirm this hypothesis. Langley[19] and, more recently, Ranson[29] have shown that this ganglion and all other parts of the cervicosympathetic do not contain sensory fibers, which on the contrary go in great numbers through the stellate ganglion. The removal of the superior cervical ganglion, therefore, would be a *pure motor operation.*

How then can one explain the result obtained? We fail to see how the resection of a very small part of the motor fibers of the heart, such as those contained in the superior ganglion, could account for the disappearance of crises of angina pectoris. The only explanation which we can offer is that such an operation paralyzes some motor fibers, thus preventing reflex accelerations, hyper- or hypotensions. The influence of the sympathectomy, in this case, would be very indirect. If one carefully examines the heart, pulse, and the blood pressure after such an operation, one will see no radical change from the preoperative findings. After the removal of the superior cervical ganglion we have found nothing to indicate paralysis of the motor fibers of the heart, and for this reason we have seen fit to reject this theory. On the other hand, Frank insisted that the cervical sympathetic and especially the superior ganglion do contain sensory fibers. Frank's researches were harshly criticized by Langley, but in reality the differences in their opinions are not so great as one might at first imagine.

Experimentally Frank[13] has shown that electric excitation of the cephalic end of the cervical sympathetic is followed sometimes by hypertension, sometimes by hypotension, and he concluded that the superior part of the cervical sympathetic contains sensory fibers with both accelerator and depressor action upon the heart and the aorta. Following the same line of research, Langley[19] discovered that the reflex hyper- or hypopressure, following central excitation of the cervical sympathetic can be obtained only so long as the anastomoses between the vagus and the superior cervical ganglion remain intact. As soon as they are destroyed, excitation of the cephalic end of the cervical sympathetic becomes ineffectual.

Being a physiologist, Langley believed that the cervical sympathetic as a physiological unit did not contain sensory fibers, but he never denied that such fibers went through the superior ganglion. He concluded, from his own researches, that these fibers were of pneumogastric origin. In a letter addressed to Dr. Coffey and reproduced by him in his recent book[6] Langley expressed this opinion: "When the cervical sympathetic and the superior half of the superior cervical ganglion are separated from the vagus, stimulation of the head end of the cervical sympathetic has no reflex effects. It has no sensory (pain) fibers. Some sensory fibers not infrequently run to it from the vagus, a

few pass from the ganglion trunci vagi about the middle of the superior cervical ganglion, but most pass as nerve filaments from the vagus to the cervical sympathetic. They cause fall of blood pressure and some reflex movement when stimulated.''

If this explanation of Langley's be exact, all discussion concerning the existence of sensory fibers in the cervical sympathetic forms no more than the confirmation of a well-known fact, namely, that the anatomical path of the nerve fibers does not necessarily correspond with their physiological significance.

In any event, there is no doubt that there are sensory fibers in the cervical sympathetic and, if the resection of the superior ganglion cures angina pectoris, the result should be credited to the resection of the sensory and not of the motor fibers. In our operations upon human beings, we have frequently stimulated the cervical sympathetic electrically and so produced pain with a very definite, sharp, and limited topography.[22]

In our experiments the anastomoses with the vagus were not sectioned; only the continuation with the thoracic sympathetic was interrupted; therefore, we cannot say whether the excited fibers were of pneumogastric or of sympathetic origin, embryologically speaking, but we are sure that sensory fibers are present in the cervical sympathetic and this suffices for the question under consideration.

There is no doubt that if the removal of the superior ganglion cures angina pectoris, as shown by the patients operated upon by Coffey and Brown, the result is due to the section of the sensory and not the motor fibers. From this we may conclude that a pure motor operation should not be considered adequate when the relief is due to interference with the sensory fibers.

Accepting such conditions, the question of surgical treatment becomes comparatively simple. Its purpose is to suppress the centripetal fibers coming from the heart and aorta. In order to give our patients the greatest chance of a good result, this suppression should be as complete as possible. Since a great many sensory fibers go through the stellate ganglion, surgical intervention in this region would seem to be indicated. On the other hand, this ganglion contains also a great many motor fibers of the heart, the vasodilator fibers of the coronary artery, and the vasoconstrictor fibers of the lung. The question is whether it is more important in order to perform a radical, sensory operation to sacrifice the ganglion or, in consideration of the importance of the motor nerves, to conserve it. Jonnesco felt that the sacrifice was justified; Daniélopolu did not, and we are inclined to agree with the latter.

The normal function of the heart is determined by its internal innervation but the external cardiac nerves give it the ability to respond

to supplementary demands. For this reason one might logically expect that a denervated heart would not adapt itself to external conditions, and this seems to be the case.

Friedenthal[15] saw that after section of the cardiac nerves the hearts of animals did not adapt themselves to supplementary efforts, and Frey[14] found that such animals reacted abnormally to the ordinary cardiac drugs. In 1925 we published in a thesis[12] written by one of us, results of experiments showing that, under these same conditions, the rabbit's heart is not accelerated if the rabbit is obliged to run or to work. These researches were recently confirmed by Enderlen and Bohnenkamp.[11] After intrathoracic resection of the stellate ganglion, dogs refuse to work and have less resistance than normally.

When at rest all of these animals appear normal. We followed for more than two years dogs which had had both stellate ganglia removed by cervical incisions. During this time the heart remained normal as to frequency and rhythm; no important changes could be detected in the electrocardiograms with the exception of slight transitory modifications evident immediately after the operation. Daniélopolu and Marcu[9] discovered that such animals do not stand the ligation of a branch of the coronary artery so well as normal dogs, and Brandsburg[3] found after removal of the stellate ganglion histological changes in the cardiac muscle. These men experimented with dogs; our experiences with rabbits agreed with their conclusions but our studies of dogs are not yet complete.

These experiments seem to warn us against unconsidered removal of the stellate ganglion, and clinical results confirm this.

Beyond doubt the human being can live without the stellate ganglia, and their bilateral removal will not produce marked disturbances. We concede, with Jonnesco and Ionescu[18] and Mandelstamm,[25] that cervicothoracic sympathectomy does not greatly affect the electrocardiogram, the modification observed being very transitory and having no special significance. On the other hand, if a normal heart seems to support without any visible damage the bilateral extirpation, this does not seem to be the same with an abnormal one. As proof of this, we would call the reader's attention to the fact that the mortality following cervical sympathectomy for bronchial asthma is very low, while following the same operation for angina pectoris, it is very high. Moreover, in this latter disease, the difference in the operative mortality in those cases where the stellate ganglion was saved as opposed to those cases where it was sacrificed is very great and it is greater in the bilateral than in the unilateral operation. These differences were universally agreed upon by all authors who prepared operative statistics (Cutler,[7] Sarasola,[31] and Fontaine[12]); they, therefore, cannot be the whims of Fate but must be explained by the operative procedure.

There is no record of a case in which, the operation having been performed during a period of cardiac decompensation, the patient was saved by Jonnesco's method. Jonnesco himself lost two patients under such conditions. We, on the other hand, by means of inferior cervical thoracic ramisection operated upon a man suffering from very serious crises of angina pectoris, in complete decompensation with edema, an enlarged and tender liver and complete arrhythmia. After the operation this man not only did not suffer further from angina

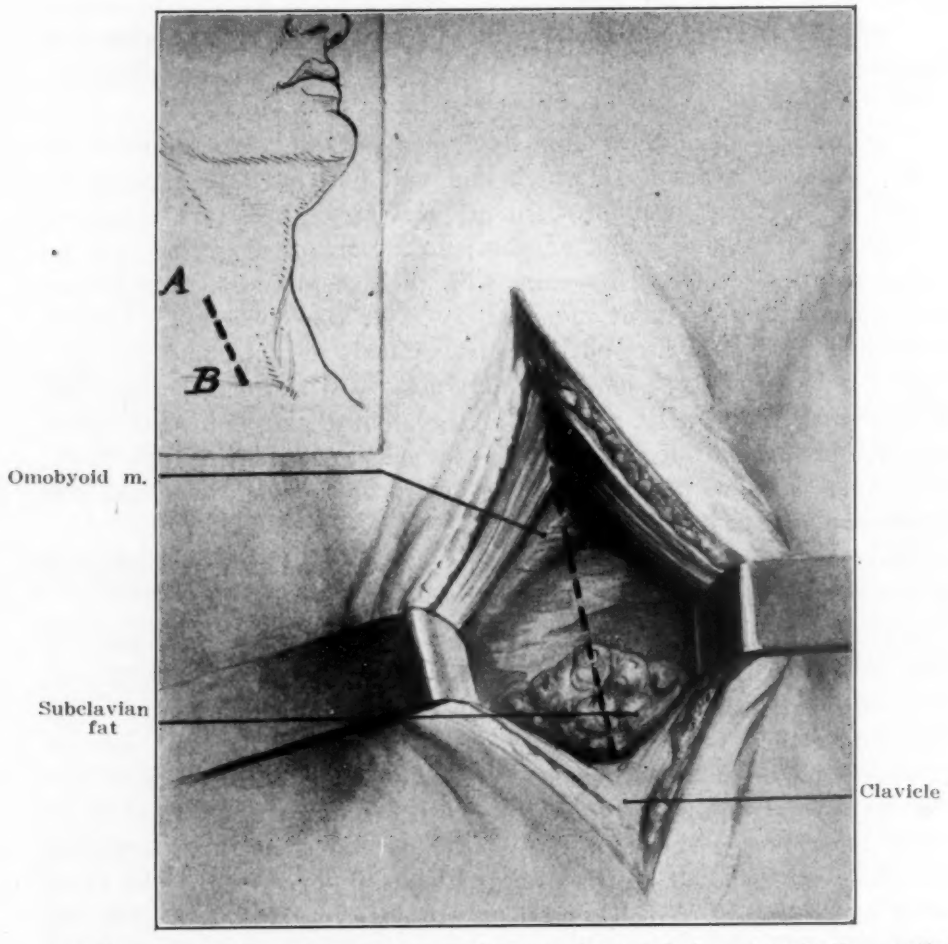

Fig. 5.—Section of the rami communicantes of the inferior sympathetic ganglion. Line of incision between the parts of the sternomastoid muscle. When the muscle is divided, the omohyoid muscle is seen in relief above, and the subclavian fat below.

pectoris, but the decompensation disappeared and the heart became regular. He died ten months after the operation from an intercurrent pneumonia. His heart remained normal until two hours before his death according to the reports from the attending physician.

The dangers involved in complete extirpation of both stellate ganglia seem very real to us. We are absolutely convinced of this after observing sudden but transient asystole in a patient soon after the

bilateral removal. This patient was a young girl suffering from essential tachycardia of nodal origin. We extirpated first the right and then the left stellate ganglion. The attacks of tachycardia were favorably affected by these interventions but several days after the second operation an asystole was observed. The patient recovered but since then we have remained convinced that the removal of the stellate ganglia in patients suffering from cardiac disease is a very daring procedure. In angina pectoris the heart is rarely normal and we, therefore, feel that this ganglion should always be saved.

But can we interrupt the sensory fibers of the heart going through the inferior cervical nervous intersection without removing the stel-

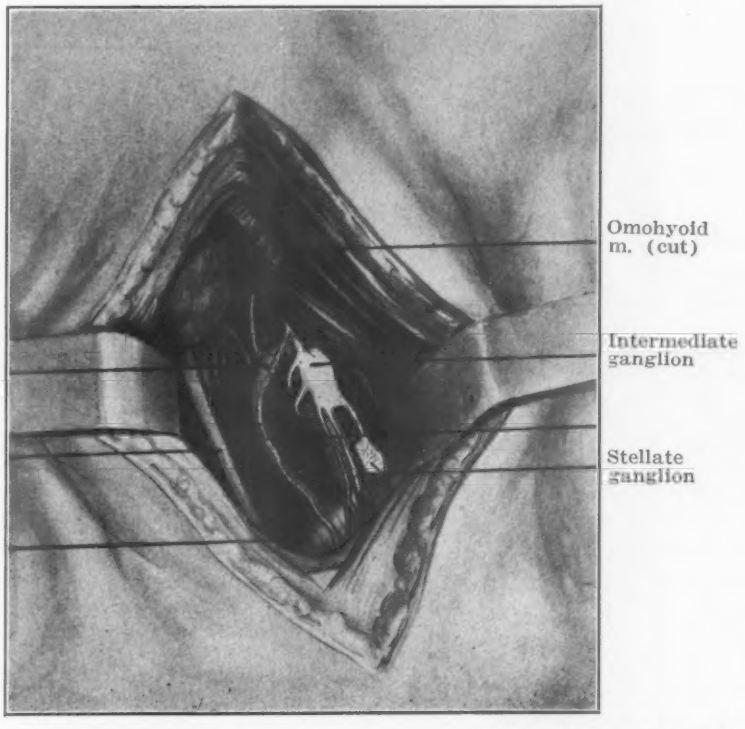

Fig. 6.—The stellate ganglion is seen deep in the wound immediately behind the vertebral artery which lies behind the thyroid artery. The intermediate ganglion lies upon the vertebral artery.

late ganglion? François Frank stated that the sensory fibers to the heart may be divided into three groups: 1, those in the cervical group; 2, those in the vertebral nerve; and 3, the superior dorsal group which is the most important. The fibers of this last group pass through the stellate ganglion and enter the spinal cord through the rami communicantes, eighth cervical to fourth dorsal.

In addition to these, others fibers, more particularly those connected with the aorta, are found in certain branches of the vagus for the most part anastomosed with the sympathetic nerve. In the rabbit and the cat these form the depressor nerve. In the human being and

the dog they are inconstant. We doubt that in the human being the depressor can always be anatomically isolated, and personally we have found it in only 30 per cent of our dissections.* Other authors who have tried to dissect it have reported similar difficulties. Where it does exist, its anatomical form varies depending upon the individual subject; it is, therefore, really doubtful whether the so-called depressor in human beings corresponds to a well isolated anatomical formation. For this reason we feel that its resection cannot be considered a well chosen method for the surgical treatment of angina pectoris as has been advocated by Hofer and Eppinger.

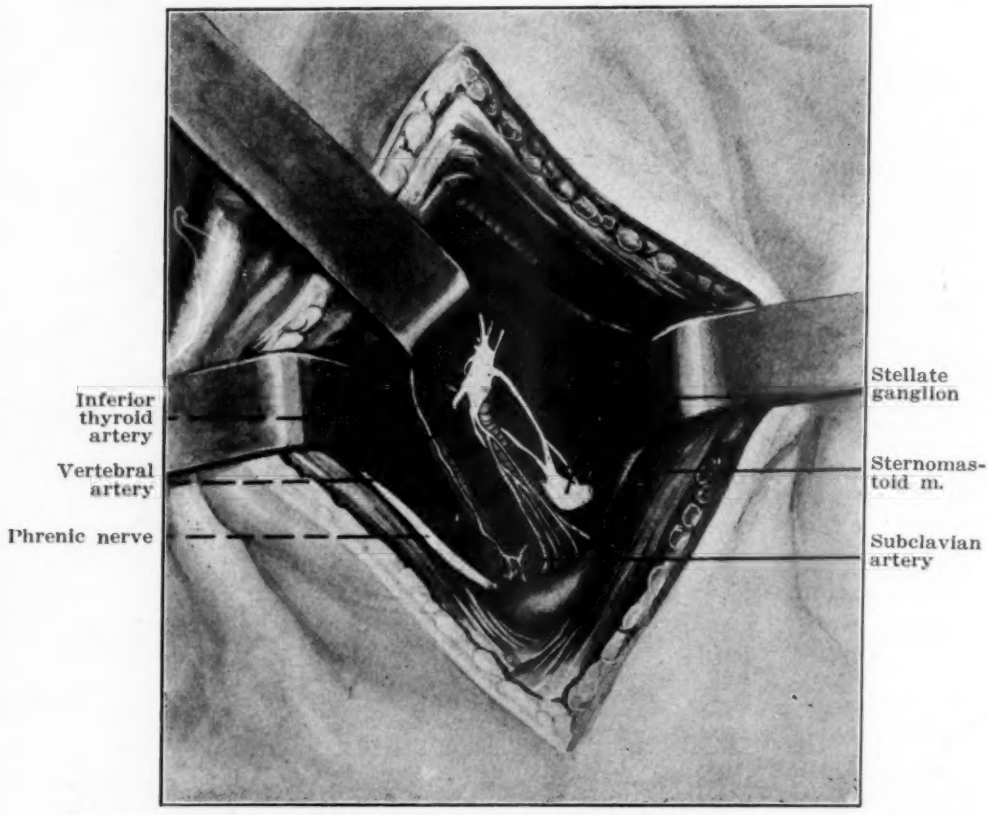

Fig. 7.—Traction on the inferior thyroid artery and the vertebral artery delivers the stellate ganglion into the wound.

There is another reason why this method should not be given preference. Wenckebach has made the statement that he believes that angina pectoris is always due to an aortitis. This theory, while very ingenious, has not been firmly established but it reminds us that the possibility of a diversified origin must always be considered.

This does not mean that we are absolutely opposed to the section

*If there is a real depressor, its electric excitation should be followed by a marked drop of the blood pressure; to our knowledge until the present time only Jonnesco and Ionescu were able on one occasion to isolate a vagus branch the excitation of which produced the characteristic modifications. Staehelin and Hotz in a case reported by Odermatt[28] were not successful.

of this nerve. On the contrary, we believe that its section is indicated whenever one finds it in performing a cervical sympathectomy for angina pectoris, but, since we are convinced that the surgical treatment should aim to interrupt as far as possible all of the sensory fibers of the heart, we feel that the section of only the depressor is insufficient.

For the same reason, in spite of their practical results, we do not hesitate to say that we consider Coffey and Brown's method of resecting only the superior cervical ganglion unsatisfactory.

Up to the present time the only failure in our own surgical treatment of angina pectoris which we have observed was in an abnormal case. A marked obesity necessitated our limiting our intervention to the removal of the upper cervical ganglion. The patient was not relieved by the operation.

In numerous papers Daniélopolu has considered all the possibilities involved in the surgical treatment of angina pectoris. His work is too well known to make it necessary to go into further detail; we shall, therefore, try to limit ourselves to our own ideas.

The majority of the cardiosensory fibers pass through the stellate ganglion, and it would seem wisest to reach them at the central point, realizing at the same time that it is necessary to save the motor fibers. This double purpose can be accomplished by cutting only the rami communicantes which go to the stellate ganglion. Such an operation interrupts the connections between this ganglion and the spinal cord. These rami do not contain any motor fibers for the heart, and for this reason we feel that the section of the inferior rami is the most important part in all operations for angina pectoris. In agreement with Daniélopolu's method we complete the procedure by cutting the cervical trunk directly above the stellate ganglion and by interrupting the vertebral nerve and finally, if present, the depressor. This procedure should not be considered strictly invariable. We occasionally modify it. The only thing that we feel should always be done is the section of the rami communicantes of the stellate ganglion in order to divide the sensory fibers which are so numerous in these nerves.

When the inferior cervical ramisection has been performed, a great number of complementary procedures are at the disposition of the surgeon. All are justified in some manner. It is possible to do (a) a suprastellate sympathicotomy, (b) section of the vertebral nerve or of the depressor, (c) removal of the superior cervical ganglion or the whole superior cervical sympathetic.

The choice of the complementary procedure depends upon the personal opinion of the surgeon governed by the gravity of the case. The most serious should receive the most extensive treatment.

On principle we avoid, as far as possible, removal of ganglia, not because the removal of these—other than the stellate—seems danger-

ous to us, but because experience has taught us that this procedure is frequently followed by pain in the cervicofacial region. We think that this occurs in about 25 per cent of all cases. Sometimes the pain is so intense that it resembles *tic douloureux de la face*. In other cases, after removal of the cervical sympathetic ganglia, hyper- or hypoesthesia was observed. Some patients suffered from pharyngeal or laryngeal disturbances and muscular atrophies were frequent. Sometimes these were quite marked. As we have elsewhere discussed these complications in detail,[22] we shall content ourselves by saying that our own experience has convinced us that they are less frequent and less intense after ramisection, and for this reason we avoid the extirpation of ganglia whenever possible.

SUMMARY

In summing up our ideas of the surgical treatment of angina pectoris, we may say that this method of treatment seems to us to be perfectly justified on condition that only carefully diagnosed cases are submitted to it. Contrary to current opinion, we believe that it is indicated in early cases before they become too advanced, too severe, and while the organ can be considered sound. In very severe and far-advanced cases, we recommend palliative treatment, such as paravertebral injections of alcohol and novocaine with which Mandl[24] in Austria and Schwartz and Swetlow[32] in this country have obtained good results.

The surgeon who decides to operate upon a case of angina pectoris should have firmly established in his mind the following principles:

1. This treatment purposes to interrupt the pathway of the reflexes which cause the crises. It, therefore, becomes a part of neurosurgical treatment and as such needs a most meticulous execution.

2. The object is to cut the ascending fibers from the heart and the aorta. Section of the motor fibers is not only useless but may prove dangerous. This dictates the wisdom of preserving the stellate ganglion.

3. The sensory fibers of the heart form different groups. Some are present in the superior cervical ganglion and in the cervical sympathetic trunk. They do not seem to be very numerous. The depressor nerve is very irregular in the human being and the existence of sensory fibers in the vertebral nerve has been discussed elsewhere (Daniélopolu, Langley).

4. The most important group of sensory fibers coming from the heart are those which enter the stellate ganglion. It is possible to interrupt this without any damage to the motor fibers by cutting the rami communicantes of this ganglion. This seems the most important part of the operation. When this section has been done, the operation may be completed in one of several ways, varying from simple supra-

stellate sympathicotomy to the complete removal of the superior part of the cervical sympathetic system avoiding in so far as possible ganglionary removals which frequently produce very disagreeable postoperative complications. The section of the so-called depressor nerve is useful if one is able to identify it, and it is wise to interrupt the vertebral nerve if possible.

Cervicothoracic ramisection being, we believe, the most important part of the surgical treatment, we should like to give some details of our method of operating. The operation is delicate but not dangerous, and it is easily performed under local anesthesia (Figs. 5, 6 and 7).

We prefer an incision about six or seven centimeters in length which divides both parts of the sternocleidomastoid muscle. The middle cervical fascia is then opened and the omohyoid muscle which is included in this fascia is divided. The vessels are then retracted to the inner side of the neck and the inferior thyroid artery is dissected. It is usually unnecessary to ligate it. Posterior, but in the same direction, one can then easily find the vertebral artery. On its anterior side the prevertebral sympathetic is disclosed. We think that it is difficult to find this nerve before reaching the vertebral artery. The anterior portion will be readily found in front of the thyroid artery but most of the branches of the prethyroid sympathetic enter freely into the thorax and can thus mislead one. We have always found it better to search at once for the vertebral artery. On the anterior side of this there is sometimes a small, sometimes a very large, ganglion. This is not the stellate but the intermediate. The stellate ganglion is located behind the vertebral artery and one must retract this toward the external side in order to find the stellate which is on the posterior and inner side of the vessel. In order to dissect this ganglion in its entirety, it is necessary to go into the thorax as deep as the second rib. After correctly identifying the rami communicantes, we cut them separately. These are the ones which come from the external side of the stellate ganglion.

If one operates upon the left side, what should always be done first in the surgical treatment of angina pectoris is to watch carefully lest one accidentally cut the thoracic duct which can easily be identified and avoided.

In concluding this paper, we should like to emphasize the fact that the surgical treatment of angina pectoris still remains open for discussion. The best method is still to be found. Experimental studies on animals are of little value now because they can answer questions of only secondary importance. Real advance along this particular line can only come from greater experience and for this reason we must have very carefully studied observations. Only when we have at our disposal reports based upon an extensive and carefully collected clinical material can we hope to answer the question as to which

is the least dangerous and at the same time the most effectual method. As angina pectoris is not a very common disease, no surgeon can reasonably expect to acquire sufficient surgical experience to answer all of the questions arising in this connection. For this reason all surgeons who have done such operations should publish their complete observations in a precise and uniform manner, so that some day some one may balance the results and arrive at some conclusions as to what is the most satisfactory method to follow in the surgical treatment of angina pectoris.

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THE ASSOCIATION OF ANGINA PECTORIS AND HYPERTHYROIDISM*

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ANGINA pectoris was described originally by Heberden,[1] an Englishman, in 1768 in a lecture before the Royal College of Physicians in London. The term was derived from the chief characteristic of the disturbance, namely, "a strangulation of the chest or breast." So complete and accurate is Heberden's original description of what is now among the most common disorders of the present day, that little may be said to have been added to it in the past century and a half, with the exception of that gained through modern laboratory developments and studies. Angina pectoris is no doubt on the increase, possibly it is recognized more often now, but it is more likely that the increased pressure in our present mode of living predisposes to the condition.

Is angina pectoris a clinical entity or disease or is it a symptom complex with variously involved causative factors? The opinion of most writers is that it is a symptom complex, but Allbutt[2] in his exhaustive work on the *Diseases of the Arteries Including Angina Pectoris* is quite emphatic in calling it a disease and not a symptom. We hold with the former view and consider angina pectoris a syndrome or symptom complex caused by various underlying conditions, characterized by substernal pain, pressure or choking sensation, which is paroxysmal in character, brought on usually by effort, often by mental excitement and often without any demonstrable cause, the pain frequently radiating down the left arm and relieved by rest and nitrites. The condition is more common in men than in women, occurs usually after the sixth decade of life and is often associated with some degree of vascular sclerosis. The fear or feeling of impending death, the so-called "angor animi" during an attack, on which great stress is laid by textbooks, has, in our experience, at any rate, not been such a prominent feature. Individual cases may, of course, show any, or all, or any degree of the above mentioned group of symptoms.

The literature abounds in reports on angina pectoris in its various manifestations and its occurrence in association with other diseases. Thus, there are reports on its occurrence in arteriosclerosis, syphilis, hypertension, anemia, gout, diabetes, etc. The occurrence of angina pectoris in hyperthyroidism would seem to be rare, judging from the relatively

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few reports on this particular combination in the literature.* We have been unable to find reference or mention of it in Osler's[3] *Lumelian Lectures on Angina Pectoris* or in Allbutt's book. Levine,[4] in his report of 103 cases of angina pectoris studied at the Peter Bent Brigham Hospital, does not mention thyroid disease. Neither does White[5] speak of thyroid disturbance in his recent review of angina pectoris in *Nelson Loose Leaf Medicine.*

Its occurrence, however, has been observed by a number of workers. Mackenzie[6] reports one case of a man, aged thirty-six years, with exophthalmic goiter and marked symptoms of angina pectoris. Following recovery from his thyroid disturbance, the man had remained free of anginal symptoms for fourteen years. Hirschfelder,[7] in writing on associated clinical conditions in angina, speaks of vasomotor anginas as associated with hyperthyroidism and exophthalmic goiter. He cites the case of a woman, twenty-three years old, with Basedow's disease and angina pectoris. The patient refused surgery and disappeared from further observation. Sturgis[8] reports the case of a woman, aged fifty-five years, with angina pectoris and exophthalmic goiter who, after surgical intervention, remained free of anginal symptoms for two years and was able to return to work which she had been forced to give up because of her chest pains. Note that two out of the three cases cited are women and also the comparative youth of two of them —thirty-five and twenty-three years.

In connection with our present discussion it is interesting and instructive to review briefly recent reports of angina pectoris occurring in patients with myxedema when put on thyroid medication. Means, White and Krantz[9] cite one case of a man, fifty-six years old, with myxedema, who, when given thyroid, showed improvement of the myxedematous condition but who developed substernal pain on effort necessitating the stopping of his thyroid medication. When thyroid medication was discontinued, the anginal symptoms disappeared, and those of myxedema reappeared. Fahr[10] had a similar experience with one of his myxedema patients. In one of our own cases of myxedema seen recently at the Michael Reese Hospital, as much as fifteen grains of thyroid were given in a day. No anginal pains developed, but there did develop an auricular fibrillation with a general ill feeling so that the thyroid medication had to be stopped.

In contrast to such type of cases is the one reported by Sturgis[8] of a woman fifty years old with definite stigmas of myxedema who was having typical attacks of angina pectoris. When given thyroid the cardiac condition became much worse, necessitating stopping the thy-

*Leube (1908) mentions attacks of palpitation associated with feelings of anxiety closely resembling the picture of angina pectoris. George Dock in Osler's *Modern Medicine* (1909) comments: "stenocardia, even typical angina pectoris has been observed, but may be a complication." Dieulafoy (1911) says, "in some cases the symptoms of angina pectoris have been recorded."

roid treatment. Another case by the same author is that of a man, aged fifty-seven years, in whom the same condition was experienced.

In obtaining the histories from our patients we were rather struck by the fact that in the majority of instances the chest pain was not one of the chief presenting complaints. On being asked, however, whether pain was ever present or not, the patients were quite emphatic about its past existence and vividly recalled the substernal and chest pains to be described presently. Our assumption is that the nervousness, weakness, tremors, palpitation, tachycardia, etc., are so much in the foreground when the patient applies for medical attention that previous attacks of chest pains are temporarily submerged and forgotten. It may also be that as the hyperthyroidism increases, the patient's physical activities are reduced, thereby decreasing the likelihood of the occurrence of anginal pains so that the patient more or less forgets them. In this respect it resembles the disappearance of anginal symptoms in those of its victims who later develop cardiac decompensation. May this not be one of the reasons why angina pectoris would seem to be so relatively rare in hyperthyroidism? We believe that, bearing its possibility in mind, closer questioning of hyperthyroid patients will not infrequently disclose the association of angina pectoris.

With these few preliminary statements we are ready to give our case reports:

CASE 1.—Mrs. E. R., housewife, aged fifty-one years, entered the Michael Reese Hospital January 25, 1928, with a history of enlargement of the thyroid for twenty-two years; loss of weight, nervousness, weakness, tremors, etc., for past year and a half. In addition, in the past few years, she had been subject to recurring attacks of substernal pain and pressure, as if the chest were in a vise; the pain frequently radiating down the left arm. These attacks generally came after exertion and walking, especially after a meal and in cold weather. During an attack she had to stop and lean against something until the pain became less severe, which generally occurred in from three to five minutes. There was marked difficulty in breathing during an attack. Following the attacks the hands and arms felt weak and there was numbness from the hips to the knees. In the past year, the chest pains have been less frequent and less severe, with the exception of the past month when she had three severe spells during the cold and snowy season when walking was difficult. Nitroglycerin had never been tried. Examination showed a moderate exophthalmos and a small, firm nodule 3 by 2 cm. in the right lobe of the thyroid. The heart was enlarged to the right and left with presystolic and soft systolic bruits at the apex. Liver dullness extended two fingers' breadth below the right costal arch, and there was tenderness on pressure. Blood pressure was 160/90; an electrocardiogram taken on February 3, 1928, showed a sinus tachycardia with a rate of 115 per minute; A-V conduction time was 0.20 seconds; there was a marked delay in conduction through the ventricles; the damage seemed to be more marked in the right ventricle, giving rise to a left ventricular preponderance. The curve resembled, although it was not typical of, a right bundle-branch block. A metabolic rate on the day after admission was 59.8 per cent above normal. Diagnosis: toxic thyroid. Under Lugol's solution

and general hospital management the basal metabolism rate decreased to +8 per cent on February 13, 1928. On the next day thyroidectomy was performed. At the present writing the patient is making an excellent postoperative recovery. The postoperative electrocardiogram showed a sinus rhythm with a rate of 75 per minute; A-V conduction time was 0.20 sec.; marked delay in conduction through the ventricle amounting almost to a right bundle-branch block; the auricular waves in all leads showed some notching, especially in the first, marked left ventricular preponderance. The indications were those of advanced myocardial degeneration or sclerosis. It is, of course, too early to predict the effect of the operation on the substernal pains.

CASE 2.—Mrs. I. H., housewife, fifty-nine years old, with a marked exophthalmic goiter, complained of recurring attacks of "heart pain" which she had been having ever since a severe attack of scarlet fever when thirty-eight years of age. The attacks consisted of severe, sharp, grinding pain in the left chest and under the sternum, coming usually after walking in cold weather or against a cold wind. Pain did not radiate. During an attack the patient had to stop and rest until the pain let up. In the past two years the attacks have been more frequent and more severe. The past history is negative except for frequently recurring attacks of bronchitis and asthma. In addition to the marked exophthalmos and diffuse hypertrophy of the thyroid gland the following were also noted: marked tremor of hands; left heart border, 9.5 cm. from midline; right heart border, 2.0 cm.; soft systolic murmur at the apex; blood pressure, 188/92; white blood count 9700; the metabolic rate was only 2.1 per cent above normal, but the test was unsatisfactory because of the patient's general restlessness and difficulty in breathing at the time. An electrocardiogram showed a slight left ventricular preponderance and notching of the auricular complexes in Leads II and III, suggesting some interference in spread of the conduction wave through the auricle. On January 10, 1928, thyroidectomy was performed under ethylene anesthesia. The microscopic report on the tissue removed reads: "Degenerated colloid pseudo-adenoma of the thyroid with fibrosis and calcification." This patient had a rather severe postoperative course, developing a bronchopneumonia and a pronounced psychosis. She recovered, however, and left the hospital in good condition on February 6, 1928.

CASE 3.—Mrs. A. B., housewife, fifty-nine years old, with exophthalmic goiter, entered the Michael Reese Hospital February 2, 1927, after having had a single polar ligation several months previously at another institution. This patient gave a history of having had recurrent attacks of pain in the left chest for a period of many years. The attacks came usually after some physical effort and consisted of severe, sharp pain in the precordium, the pain often going down the left arm and occasionally also down the right. Nitroglycerin gave relief, as did also rest during an attack. These cardiac pains we learned later on had so impressed the surgeon that he was afraid to do anything more than a polar ligation at the first operation and the patient now sought further relief largely, if not entirely because of the anginal pains. The patient had marked exophthalmos. There was moderate enlargement of the thyroid, of the right lobe more than the left; marked tremor of the hands; the heart had a transverse diameter of 14.5 cm. and there was a soft systolic blow at the apex; blood pressure 154/76 mm.; Hb. 80 per cent, R.B.C. 4,670,000, W.B.C. 8400; Wassermann negative; initial metabolic rates were 46.2 per cent and 39.4 per cent above normal. An electrocardiogram showed a sinus rhythm, P-R interval 0.12 seconds, with T_1 diphasic, T_2 isoeletric, and T_3 inverted. Under Lugol's solution, etc., the patient's condition improved so that on March 30, 1927, a subtotal thyroidectomy was performed. The pathological report was "colloid goiter with subacute and chronic

perithyroiditis.'' A postoperative electrocardiogram showed T_2 of high voltage and T_3 upright. The patient made a rapid, uneventful recovery, leaving the hospital on April 7, 1927. We have seen her from time to time in the past year. There has been no recurrence of her chest pains to date.

CASE 4.—Mrs. A. J., sixty-two years old, entered the hospital on November 14, 1926, with a history of having received x-ray treatments a month previously for a toxic thyroid. Her complaints at that time were loss of weight (25 pounds in five months), nervousness, tachycardia, insomnia, and an occasional pain in the left arm. In addition to an increase in the severity of these symptoms, she now made an additional complaint of having developed severe epigastric and precordial pains in the last two weeks. The pain came on generally after meals and radiated down the left arm. The attacks were often associated with gaseous distention, belching, and passage of flatus. Metabolic readings on this admission were 35.7 per cent and 29.6 per cent above normal. Under bed rest she felt sufficiently improved to leave the hospital three weeks later.

She reentered the hospital again on March 13, 1927, with a history of more marked recurrence of all her previous symptoms, especially the attacks of epigastric and precordial pains. The patient now recalled also that in the past year she had had a number of attacks of ''stopping of the heart,'' with fainting and loss of consciousness for one to two minute periods. Examination now showed a nodule in the isthmus and left upper lobe. The heart was enlarged to the left and was fibrillating. Liver and spleen were negative. Blood pressure was 180/110 mm. An electrocardiogram confirmed the auricular fibrillation and in addition showed a left preponderance and a high T_1. The metabolic rate was 26.6 per cent above normal. Diagnosis: hyperthyroidism, paroxysmal auricular fibrillation, and angina pectoris. On March 29, 1927, a thyroidectomy was performed. The pathological report reads ''multiple degenerated fetal adenoma of the thyroid gland.'' The patient left the hospital twenty days after the operation. There has been no recurrence of the epigastric and precordial pains.

CASE 5.—Mrs. F. Z., housewife, forty-nine years old, entered the hospital on December 28, 1927, complaining of nervousness, loss of weight, and pain in the chest of from six to eight weeks' duration. The pain was severe and squeezing, especially over the sternum and just below the jugulum. Occasionally the pain radiated down the left arm. The attacks occurred usually after a big meal and after walking. There was no dyspnea. Past, personal, and family history were negative. Examination showed the eyes to be staring but there were no other ocular signs of Grave's disease; there was a hard nodule in the left lobe of the thyroid. Heart and lungs were negative. Hands showed a marked tremor. Blood pressure 152/74 mm.; urine negative; blood count showed a moderate secondary anemia. A distance heart plate showed a transverse diameter of 13.8 cm. Two metabolism readings were 57.7 per cent and 36.6 per cent above normal. An electrocardiogram was not made. Diagnosis: exophthalmic goiter. Lugol's solution, M.x, three times a day was prescribed. The patient left the hospital a week later against the advice of her physician. She continued doing poorly at home and had frequent recurring attacks of her chest pains which even interfered with her sleep at night. Her physician advised surgery of the thyroid, but she refused and instead went to seek another medical opinion. On leaving the second doctor's office one day, she refused to ride down in the elevator and instead walked down eighteen flights of stairs to the street. The following day she had a sudden hemorrhage from the mouth and died before medical aid reached her. There was no autopsy.

CASE 6.—M. T., male, fifty-six years old, manager for a diamond concern, entered the hospital for the first time on August 15, 1927, complaining of loss of weight (20 pounds in eighteen months), asthma for years, nervousness, increased perspiration and dyspnea on effort in past two or three years. In the past year he had been having a feeling of tightness and constriction around the chest and abdomen, even on very slight exertion, and would tear at his clothes in an attempt to relieve the constriction. Belching was prominent during an attack as was also an intense desire to urinate and defecate. Nitroglycerin had not been tried during an attack.

Examination at this time showed the patient to be quite dyspneic, with cyanosis of the lips and cheeks. Slight exophthalmos; marked tremor of hands; small nodule in the left lobe of the thyroid; chest was emphysematous with numerous râles anteriorly and posteriorly; left heart border, 12.5 cm. from midline; right heart border, 5.0 cm.; there was a slightly roughened, short, systolic murmur at the apex with an occasional extra systole. Abdomen was negative; blood pressure 166/128 mm.; white blood count 10,900; Wassermann negative. Two metabolism determinations were 59.1 per cent and 43.3 per cent above normal. Diagnosis: hyperthyroidism, coronary sclerosis (?), emphysema. Patient improved in the hospital and a subtotal thyroidectomy was done. Microscopic report was "colloid thyroid with fibrosis." The man left the hospital on September 14, 1927, feeling much improved.

He entered the Michael Reese Hospital for the second time on October 4, 1927, saying that for two weeks after his operation he felt quite well, after which he again developed cough, dyspnea, and orthopnea. No mention of chest pains was made on this admission. The findings were essentially the same as before. Under digitalis he improved sufficiently to leave the hospital eight days later and return to his business.

His third and final admission was on October 29, 1927, because of recurrent and more pronounced cough, dyspnea, and orthopnea. Examination now was about the same as before, except for the presence of a slight edema of the ankles. The blood pressure was a little lower, 142/96 mm., and the white blood count, 11,200. Under digitalis and ephedrine, the man improved for a short time. A note on the chart made by the senior intern on November 11, 1927, reads, "patient complained of severe numbness and tiredness in the region of the left elbow all day. At 6:30 P.M., this changed to a severe pain which radiated up the arm to the precordium and through to the scapula. Patient restless and given morphine, gr. 1/6, and felt relieved."

From about this time on the patient's general condition began to fail, and he had numerous recurrent severe attacks of pain over the precordium and right chest which required morphine for relief. Edema became more pronounced and there was tenderness on pressure under the right costal arch. On November 24, 1927, the patient suddenly developed a severe pain in the left shoulder which was not relieved by morphine. A few hours later, while trying to urinate, the patient suddenly collapsed and died.

An autopsy was performed nine hours after death.

The heart was enlarged to the right and left measuring 20 cm. in the transverse diameter. On the anterior surface of the left ventricle near the inter-ventricular septum a slight bulge was apparent and on palpation this area felt quite cystic as compared to the surrounding cardiac tissue. On opening the heart the mitral and tricuspid rings were found to be stretched. The bulging area noted on the surface of the heart was seen to be an aneurysmal-like thinning of the ventricular wall measuring 2 cm. in diameter and filled with a recent thrombus. The ventricular musculature was distinctly hypertrophied and many grey streaks of

fibrous tissue could be seen. There were also several placques of scar tissue 0.5 to 1 cm. in diameter present in the myocardium. The endocardium was thin and smooth. The papillary muscles and chordae tendiniae were not hypertrophied. There was a slight degree of arteriosclerotic change in the mitral valve. The tricuspid and pulmonary valves showed no change. The right ventricular wall was slightly hypertrophied. The aortic cusps were thin but the root of the aorta contained many small, yellow, ring-like and longitudinal placques.

Section of the coronaries showed a very definite degree of atheromatous change. The first part of the anterior descending branch of the left coronary artery showed an especially marked degree of sclerosis for a distance of about 3 cm. from its origin at which point the lumen was very definitely narrowed. Just preceding this point a branch of this vessel which leads to the area of ventricular infarction mentioned above was markedly sclerotic and shortly after its origin the lumen was almost obliterated. The heart weighed 880 gm.

Microscopic sections of the heart showed distinct hypertrophy of the musculature with loss of staining qualities. In many sections there was proliferation of fibrous tissue. In all the sections studied, the smaller branches of the coronary arteries showed normal unchanged structures, but the larger vessels invariably showed a thickening of the intima varying in degree in different sections; in some being so marked as to cause almost a complete obliteration of the lumen.

Examination of the other organs of the body revealed nothing of consequence for our present subject.

DISCUSSION

The cases herewith presented bring up a number of interesting problems and questions for discussion. First, it may be questioned whether these cases may be considered "true" angina pectoris; and immediately one asks—what is "true" angina pectoris? For example, there are many cases of paroxysmal, severe, precordial pain which may be considered anginoid in character, but which are in a sense different from the angina of effort; for example, the paroxysmal pain which often accompanies the attacks of paroxysmal tachycardia and fibrillation; the angina of mitral stenosis, particularly with decompensation; the recurrent attacks of angina of aortic insufficiency in young people; the angina, aortalgia, of active rheumatic aortitis in children; the angina of arteriosclerosis or luetic aortitis; the angina of exhaustion or beginning heart muscle failure, frequent in old hypertensive hearts, and in young people following acute fever and infections, influenza, etc. What relationship, if any, exists between these types of paroxysmal pain and the angina of hyperthyroidism? Are there any inherent factors in hyperthyroidism which of themselves are particularly apt to precipitate attacks of angina? If so, why do not all patients with hyperthyroidism suffer with angina pectoris, or, at least, why is it not more frequent?

In light of our present knowledge we would answer these several questions by stating our present conception of angina in hyperthyroidism as follows, with the understanding, of course, that such statements are tentative and that as new cases and knowledge, particularly evi-

dence from post-mortem examinations accumulates, they may have to be modified, broadened, or contraverted entirely. In general we conceive the paroxysmal pain of angina pectoris, from any source, to be due to an ischemia or anoxemia of the heart muscle. In hyperthyroidism, with its usually constant tachycardia, with its increased metabolic rate, with the increased oxygen consumption, with all the vital forces of the body speeded up, comparable to that during active exercise, the increased demands on the heart muscle are considerable and must be met. If these can be met satisfactorily, no pain develops. If they cannot, ischemia or anoxemia of the heart muscle occurs and pain develops. We would postulate, therefore, that in those cases of hyperthyroidism, free from angina, the coronary blood supply is sufficient for the need of the actively working cardiac musculature and coronary sclerosis is absent or minimal, while in those cases of hyperthyroidism with angina, the blood supply is insufficient, either from coronary sclerosis, anemia, or both, and angina is present and demonstrable. In the cases of hyperthyroidism with severe protracted angina and sudden death, coronary occlusion and infarction can usually be demonstrated, as witness our last case.

The practical importance of this concept to pathogenesis and treatment (surgical interference) needs a word. From the standpoint of the former, the constantly increased metabolism and the harmful effects of the hyperthyroid activity affect both heart muscle and its vascular supply deleteriously. Therefore, the earlier this is recognized and corrected, the less widespread myocardial and vascular damage. From the standpoint of surgical interference the removal of the offending, toxic goiter (the "whip" of the already diseased muscle) is urgently indicated provided such removal can be accomplished safely. In the evaluation of this latter factor, electrocardiographic evidence of the degree of coronary and myocardial damage is helpful.

The criticism has been advanced that these cases are not cases of "true" angina pectoris, the angina of Heberden, but that they are merely cases of thyroid disease with chest pain. We would reply that we have excluded a much larger series of hyperthyroidism with no or indefinite or vague chest pains, and are restricting this discussion to these few cases in a series of well over one hundred as cases of "true" angina pectoris in association with hyperthyroidism. We hold with Paul White that "angina pectoris is a paroxysmal thoracic oppression, usually substernal, brought on chiefly by exertion, occasionally by some functional disturbance of cardiovascular origin, and generally associated with coronary or aortic sclerosis" and that "all angina pectoris is true angina pectoris."

In the classification of Mackenzie it is helpful to consider that many of these cases of angina pectoris in association with hyperthyroidism

are cases of "secondary angina." By secondary angina Mackenzie implies the angina more frequently seen in women before or at middle age in whom the condition is curable in the sense that the attacks may cease and the patient suffer no more from heart pain; the distress is as a rule the sense of exhaustion; there are no gross changes in the heart, the pain is induced by an undue susceptibility of the nervous system due to some influence other than the heart; the attacks are often accompanied by shivering; the attacks are seemingly more violent than the condition would account for and the symptoms are more widespread, due to the extreme susceptibility of the nervous system; patients with secondary angina suffer from other ailments besides the heart condition and do not have the sense of well-being between the attacks. In this sense cases of angina in association with hyperthyroidism may well be considered as cases of secondary angina, the anginal attacks being the result or expression of the harmful effect of the thyrotoxicosis on the heart, particularly in association with the hypersensitive nervous system so characteristic of this disease.

Of course it is undoubtedly true that cases of so-called primary angina pectoris may be associated with hyperthyroidism—witness our last case—the association being merely coincidental and not in any sense causal. In such cases, however, it is obvious that the heart is being damaged from two sources, with the result that treatment, particularly surgery, may be expected to be so much more hazardous, and prognosis less favorable. One might be forgiven for considering such cases as instances of combined primary and secondary angina.

SUMMARY

1. Six cases, five women and one man, of associated angina pectoris and hyperthyroidism are included in our series.

2. One case is reported with autopsy findings.

3. The youngest individual in our series was forty-nine years, the oldest sixty-two, the average age for the six cases being fifty-six years.

4. The predominance of women in our series may be only a coincidence or it may suggest that, in hyperthyroidism, angina is more likely to occur in women than in men.

5. Of the five cases operated upon, four have remained free of anginal pain to date, one patient continued to have cardiac pains and died a month later.

6. The occurrence of angina pectoris in hyperthyroidism is not common but probably is not quite so rare as heretofore thought.

7. As to the pathogenesis of angina pectoris in hyperthyroidism, we offer the suggestion that its occurrence is evidence of ischemia or anemia of the heart muscle due either to anemia, coronary sclerosis,

or occlusion, or to some other factor or factors interfering with an adequate coronary blood supply to the actively working thyrotoxic heart.

8. The majority of cases of angina pectoris occurring in hyperthyroidism belong to the class of secondary anginas as described by Mackenzie.

9. Cases of angina pectoris associated with hyperthyroidism may properly be called "thyroid angina" just as cases of tobacco angina, angina of anemia, etc., are now recognized. In this connection it is suggested that in certain cases of angina occurring in women approaching middle age the possibility of an underlying or an associated hyperthyroidism be considered, and conversely that in hyperthyroidism occurring in such patients the possibility of an associated angina be investigated.

We wish to thank Drs. Solomon Strouse and George Davenport for the use of their records for Cases 5 and 6, respectively.

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SPONTANEOUS ARTERIOVENOUS ANEURYSM IN THE THORAX*

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SPONTANEOUS rupture of a diseased aorta occasionally occurs into the superior vena cava, the left innominate vein, or the left auricle of the heart, with the production of a train of signs and symptoms which is quite characteristic.

Recently Shennan[1] has published a critical study of this subject, collecting seventy cases and adding one of his own. He also reports a case of arteriovenous aneurysm between the aorta and the right auricle. He gives a summary of the essential features in sixty-one of these cases, the other ten records not being available for study.

We wish to add three cases from the literature to Shennan's list. Deeks and Darling[2] report the case of a white man, aged forty-six years, who first noted a swelling of the face and neck associated with a full feeling in his head. He lived thirty-four days after the onset of the swelling. Dyspnea became extreme, and the cyanosis and swelling of the upper half of the body were progressive. There was no evidence of syphilis. The veins of the anterior thorax and of the back were very prominent. There was a palpable thrill at base of the heart. There was also a double murmur. A few days before death cyanosis and edema became general, and ascites occurred. The autopsy revealed a large aneurysm of the ascending aorta measuring 13 by 11 cm. which communicated by rupture with the superior vena cava at the level of the azygos vein. There were other aneurysmal pouchings and dilatations of the aorta, and the process was spoken of as an atheromatous change, no mention being made of syphilis. There was no edema of the lower extremities and ascites is not mentioned in the post-mortem report. Sufficient details are not given in this report to eliminate the possibility of syphilis as the underlying cause.

Hartman and Levy[3] report two cases. The first of these was a negro, aged twenty-eight years, who had a sudden pain in the chest while working, followed immediately by a swelling of the face and neck. After three months he sought medical aid, and at this time there was swelling of the head, neck, and right arm, with a visible pulsating tumor to the right of the sternum. Over this tumor there was a systolic thrill and a double murmur. He died six days later, and the autopsy revealed a large aneurysm of the aorta which had ruptured

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into the superior vena cava between the right auricle and the azygos vein. Syphilis of the aorta was also present.

Their second case was a negro, aged thirty-four years, who had an epigastric discomfort while resting after lunch. Within a few moments the discomfort became substernal and a swelling of the neck was noted. Shortly afterward the patient fainted. He lived ninety-nine days after the onset. Dyspnea, orthopnea, swelling of the face and of both sides of the neck, more marked on the right, were present, and slight edema of the chest wall, abdomen, legs, feet, and right shoulder was noted. There was an area of substernal dulness over the third intercostal space, a systolic thrill, and a double murmur in the aortic area. The systolic blood pressure was 145 mm. Hg, and the diastolic pressure was 92 mm. Hg in each arm. The autopsy revealed a syphilitic and atheromatous aneurysm of the aorta which had ruptured into the superior vena cava between the left innominate and azygos veins. Bilateral hydrothorax and serofibrinous pericarditis were also present. The arteriovenous opening was situated 3.5 cm. above the azygos opening and the inside measurement of the aortic aneurysm was 7 cm.

Whether or not there was an obstruction of the azygos vein by the aneurysmal tumor is not stated, but this can be assumed as probable by the presence of hydrothorax with no other explainable cause.

We have thus found seventy-four cases of intrathoracic arteriovenous fistulae in the literature, and we wish to report in addition an instance of aortic rupture into the superior vena cava which we have observed.

CASE REPORT

E. L., a colored male, aged thirty-nine years, was admitted to the Nashville General Hospital on April 25, 1926, complaining of swelling of the face, neck, body, and arms.

Present Illness.—On the night of April 1, 1926, the patient was drinking whisky and playing cards when the right side of his face and neck began to swell. There were no particular subjective symptoms. Within five hours the entire head, face, and neck were much swollen. About two weeks later the body and upper extremities became swollen. The patient has had a choking sensation when lying down and a dryness of the mouth when sitting up, and consequently he has slept very little. There was bleeding from the nose during the first night of his illness and he has vomited three times since. Soon after the onset he was given an intravenous injection by a physician, of a solution said to be "Salvarsan." This was repeated once.

Personal History.—He had been a heavy drinker for many years. There had been no loss in weight before the present illness. His usual weight was about 160 to 170 pounds. Anorexia existed for three or four weeks before the onset of the present illness but otherwise he had been in good health.

Past History.—He stated that he had had a sore on the penis in 1914, which lasted several weeks, and this was followed in about eight months by an eruption which left scars. He had had gonorrhea three or four times. The last attack was in 1918.

Physical Examination.—On admission to the hospital the following note was made: Temperature 97° F., pulse 100, respiration 22. The patient appears to be about forty years old. There is marked swelling of the upper half of the body beginning about one inch above the umbilicus (see Figs. 1 and 2). There is no swelling below this line. The face, neck, and chest appear cyanotic.

The small superficial veins of the front and back of the thorax are dilated, distended and project above the surface of the skin. These are most noticeable on the anterior surface. There are numerous large subcutaneous veins on the back of the thorax which are both visibly and palpably distended. By compression of these vessels it seems that blood flows downward and outward in them. There is not much pitting of the edema on the back and the swelling here is less than on

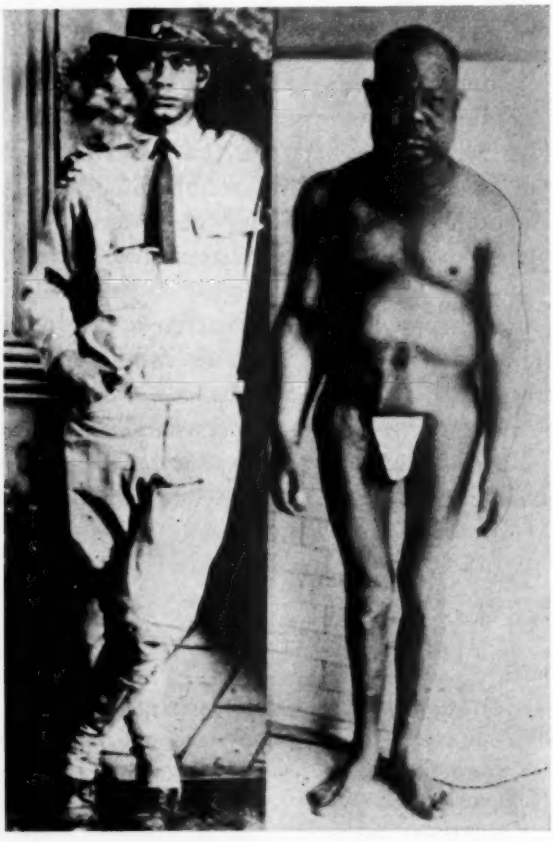

Fig. 1.—The appearance of the patient about three years before, and after the onset of the present illness. Note the lower line of swelling at the level of the umbilicus, also the enlarged veins below the umbilicus.

the front of the thorax where the pitting is much greater and the subcutaneous vessels less easily seen. There are one or two small veins on each side of the midline of the abdomen running from the umbilicus downward toward the symphysis pubis.

The edema of the arms and hands is symmetrical and pits greatly on pressure. This edema is moderately soft. The edema of the face, neck, and upper part of the chest is very firm, almost board-like. There is swelling of the inside of the cheeks, interfering with chewing. The tongue is a little swollen, dry, and deeply fissured. The voice is hoarse, suggesting edema of the larynx. The pupils are equal and react to light and accommodation.

Ophthalmoscopic examination shows very dark retinas with moderate tortuosity of the veins.

There is dulness, absent vocal and tactile fremitus and decreased breath sounds over both bases of the lungs, indicating the presence of fluid in the thorax, more in the right than in the left pleural cavity.

There is a systolic and a diastolic murmur over the aortic area, the systolic being prolonged, the diastolic short. The pulse is collapsing and the systolic blood pressure is 180 mm. Hg in the left arm and 190 mm. Hg in the right, while the diastolic pressure is 50 mm. Hg in each arm.

Fig. 2.—Showing the swelling of the upper half of the body with well defined lower limits both front and back.

The liver is very large, extending three finger-breadths below the costal margin. It is tender, and does not pulsate. There is shifting dulness in the abdomen, but apparently only a small amount of free fluid. The spleen cannot be felt.

There is a marked irregularity of the right tibia at the juncture of the lower and middle thirds. The extremities are otherwise negative. The genitalia are normal and the deep reflexes are not changed.

Laboratory Findings.—Blood Wassermann and Kahn tests were strongly positive. The urine, which had a specific gravity of between 1.022 and 1.036, showed a moderate amount of albumin and a few granular casts, but no red blood cells. The hemoglobin was 95 per cent (Tahlquist), and the leucocytes 6,850. A week after admission and following venesection the red blood cell count was 3,400,000, and the

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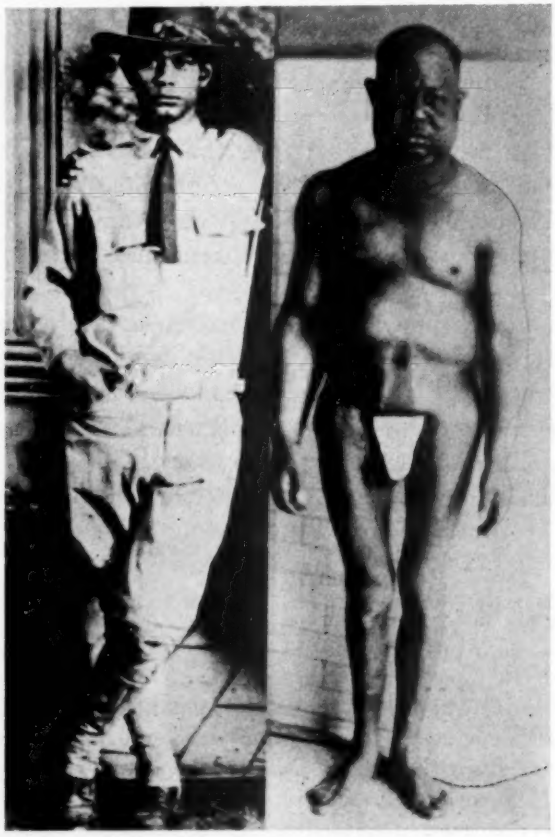

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leucocyte count was 14,600. There was no blood in the stools. The nonprotein nitrogen of the blood two days after admission was 28 mg. per 100 c.c.

The x-ray plate showed some widening of the aortic shadow, some enlargement of the heart, and suggested fluid at the right base.

Course in Hospital.—The patient died on the tenth day in the hospital. During this time he was receiving potassium iodide and calcium chloride by mouth and novasurol intravenously. Morphine was given occasionally for sleep, with fair results. Fluids were restricted as much as possible but rather unsuccessfully on account of the patient's inability to take anything but rather soft and liquid diet. The novasurol and calcium chloride did not produce marked diuresis. Venesection (500 to 600 c.c.) was performed once without any noticeable improvement. The swelling varied without any apparent cause. One day the eyes were closed entirely by the edema of the face, and the neck measured 20 inches in circumference; while on the following day the eyelids could be opened about half an inch and the neck measured 18 inches in circumference. There were also striking changes in the mental state of the patient. He became stuporous when the swelling of the head was greatest, and distinctly clearer when the swelling subsided. Marked changes in the degree of swelling were observed on two occasions to occur within two or three hours, first markedly increasing and then rapidly decreasing. There was slight edema of the left ankle for a few days before death. There was some swelling of the left half of the abdominal wall below the usual line of swelling on the day of death. On admission the engorged veins of the abdomen were mostly around the umbilicus, but after a few days these veins became less noticeable and those below the umbilicus became more prominent. The swelling of the face and neck became very great. The patient became gradually comatose and died on the thirty-fourth day of his illness.

The *autopsy protocol* is as follows: The external appearance of the body is very peculiar, there being a tremendous edema of the upper half extending uniformly from about the umbilicus involving the upper abdomen, chest, arms, neck, and head. Therefore, the upper half of the body is very greatly out of proportion to the lower half. The thighs and legs are thin. There is no edema of the scrotum. The superficial veins of the lower extremities are dilated. There is no edema of the ankles. Over the right shoulder there are cutaneous blebs so that the epidermis can in places be peeled off. The face, although previous to the present condition was said to be thin (see Fig. 1), is now rounded, and there is bulging of the eyeballs. The edema has produced a board-like hardness to the skin which pits on pressure. The pupils are equal, measuring 4 mm. in diameter. On primary incision the skin over the edematous chest cuts with considerable resistance and leaves an upstanding sharp edge. Over the chest the subcutaneous tissue measures 3 to 4 cm. in thickness. It is rigid and can be seen to be filled with fluid. Small islands of yellowish fat are separated by a pale gray, watery connective tissue. The cutaneous blood vessels are dilated and distended with fluid blood. The subcutaneous tissue over the lower abdomen where the edema is not present is thin and contains little fat.

Peritoneal Cavity.—On dissecting down to the peritoneum it can be seen before the peritoneum is opened that the anterior subperitoneal vessels extending upward from the umbilicus are enlarged, distended, and tortuous. The peritoneal surfaces are everywhere smooth and moist, but there is no excess of fluid present. The liver is hard and rather grossly nodular, and is displaced downward a hand's breadth below the costal margin in the right mammillary line. Otherwise the abdominal organs are normally situated.

Thoracic Cavity.—It is with some difficulty that the subcutaneous tissues and muscles are dissected away from the chest wall owing to the rigidity and lack of

flexibility of these structures induced by the edema. The lungs present themselves as pink and air-containing. There are about 2 liters of fluid in the right pleural cavity. There is no evidence of inflammation. In the left pleural cavity there are about 500 c.c. of fluid.

Pericardial Cavity.—Contains an excess of clear yellow fluid, about 50 c.c. in amount. The heart is moderately enlarged in the left ventricle. The epicardial surfaces are smooth except over the base of the aorta where the parietal and visceral surfaces are bound together by old fibrous adhesions.

Heart.—As the heart lies in situ with the right ventricle and auricle presenting, one can see that there is a mass, just posterior to the right auricle and superior

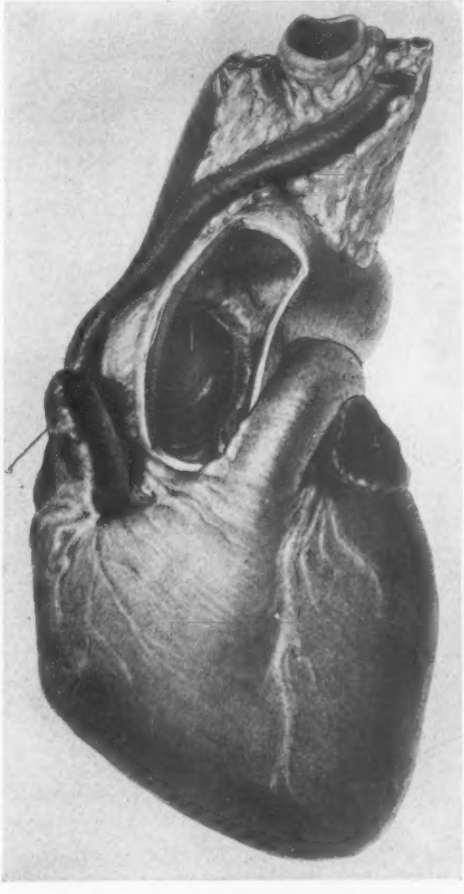

Fig. 3.—Anterior aspect of heart showing the inside of the saccular aneurysm projecting to the right and impinging on the superior vena cava.

vena cava, which is rounded and measures 6 cm. in diameter. The azygos vein on the right is greatly distended. On the left there is no evidence of dilatation of the thoracic duct. There appears to be no dilatation of the aortic ring. The aortic cusps are thin and delicate and appear to be competent. Immediately above the right posterior aortic cusp there is a spherical saccular aneurysm measuring 5 by 4.5 cm. (see Fig. 3). The orifice is oval measuring 3.7 by 3 cm. The edges are rounded and the wall of the aneurysm contains no thrombus. It is fairly smooth and pale. The aorta is dilated. It measures above the aneurysm 8.5 cm. in width. Below the aneurysm, 3.5 cm. above the left posterior cusp of the aortic valve, there is a second shallow aneurysmal sac measuring 1 by 2.5 cm. in diameter

and 1 cm. deep. The aorta itself down as far as the abdominal portion shows an irregular scarring with puckering indicative of syphilitic aortitis. In the convex portion of the arch where the left subclavian artery is given off, there is another saccular aneurysm in which the orifice of the subclavian is incorporated. It measures 3 by 2.5 cm. in diameter and 2 cm. in depth. A corresponding, but more shallow dilatation, is situated opposite this in the concave wall of the arch. In the upper part of the descending portion of the aorta on the posterior aspect there is another shallow aneurysmal dilatation 1.7 cm. in diameter, and about three-quarters of a centimeter deep. When the specimen is reversed and the superior vena cava with its branches is opened, the superior vena cava measures 5 cm.

Fig. 4.—Posterior aspect of heart showing the superior vena cava opened. The arteriovenous fistula is shown just above the constriction in the middle and opposite the impingement of the aneurysm.

across. Just as it enters the right auricle there is a constriction of the lumen (see Fig. 4) so that when opened the wall measures 2 cm. This is the point where the large aneurysmal sac just above the aortic orifice impinges upon the superior vena cava. The narrowing of the superior vena cava here is due to an adhesion of its walls by firm fibrous scars which have reduced the lumen by about half. Just above this point of adhesion there is a perforation measuring 3 by 4 mm. (see Fig. 4), and about the perforation the wall is roughened and greatly thinned. In the opening lies a stringy blood clot which extends upward into the superior vena cava and appears partly to be ante-mortem. This perforation forms

a direct connection between the aneurysmal sac and the superior vena cava. There is no evidence of mural thrombosis. The right azygos vein opens 4 cm. above the perforation, and the perforation is situated 1.5 cm. above the orifice of the superior vena cava. The tricuspid valve of the heart appears to be normal, and likewise the pulmonary and mitral valves. The myocardium has a uniform appearance, there being no evidence of scarring.

Liver.—The appearance of the liver is that of a healed cirrhosis and the coarse scarring is suggestive of the syphilitic type.

Histology.—The microscopic slides show the classical changes of syphilitic mesaortitis, otherwise the microscopic examination of the various organs reveals no additional important changes.

Final Diagnosis.—Arteriovenous aneurysm due to rupture of aortic aneurysm into superior vena cava; phlebitis of superior vena cava with partial obstruction (compression from aortic aneurysm); hydrothorax, bilateral; syphilitic aortitis; multiple aneurysms of aortic arch; hypertrophy of the heart; edema of the upper half of the body (subcutaneous); passive hyperemia and parenchymatous degeneration of the kidneys; chronic hepatic cirrhosis; focal necrosis of the liver.

COMMENT

This case is classical both as to the clinical course and the anatomical changes. Three factors were operative in obstructing the superior vena cava, namely, compression by the small aneurysm causing internal adhesions and partial obliteration of the lumen, an active "bucking" of the normal blood current by a stream from the aorta, and by the presence of a small thrombus. The increased pulse pressure and double murmur were in all probability due to the arteriovenous aneurysm, as the aortic valves were normal and the aortic ring not dilated. The hydrothorax, the swelling and enlarged veins of the back of the thorax, usually indicate in these cases obstruction of the superior vena cava below the azygos vein and such an obstruction was demonstrated in this case. There was no clinical or x-ray evidence of aneurysm other than an increased width of the aorta.

DISCUSSION

Of the seventy-five cases of arteriovenous fistula obstructing the superior vena cava referred to above, the records are not available for study in ten. Of the remaining sixty-five Shennan[1] reviewed sixty-one. We have reviewed three cases not included in Shennan's list, and added one of our own.

Sex and Age Incidence.—In sixty-three cases there were fifty-seven males and six females. These were distributed in the age groups in sixty cases as follows:

20-30	1 male
31-40	9 males, 1 female
41-50	18 males, 4 females
51-60	23 males,
61-70	3 males, 1 female

Etiology.—In all of the sixty-five cases aneurysm of the aorta was present. Syphilis was positively diagnosed or could be assumed from

the post-mortem records in thirty cases or 46 per cent. From our present knowledge of the etiology of aortic aneurysm one would suspect that syphilis had been present but overlooked in a larger number of these cases.

Symptoms and Signs.—There is usually a sudden onset of dyspnea with swelling and cyanosis of the upper part of the body. This swelling is usually greater at first on the right side of the neck and face. There is often pain or some discomfort in the chest. Suffocation, choking, strangling, constriction of the neck or in the chest, and dysphagia are common complaints. Unconscious spells of transient duration have been present in many cases.

Signs of thoracic aneurysm are often present but in many of the recorded cases the aneurysm was so small as to escape clinical detection. In our case there were no physical signs of aneurysm, although the aorta was considerably dilated.

There is often a double or continuous murmur. In sixty cases twenty-two had continuous murmurs, eighteen double, sixteen single (15 systolic, 1 diastolic), and four had no murmurs. A thrill or heaving impulse is often present at the base of the heart. That a to-and-fro murmur, with low diastolic pressure and increased pulse pressure, may result from an arteriovenous aneurysm alone without an attending aortic valvular insufficiency has been fairly well established, as in our case.

Obstruction of the superior vena cava by aneurysms and other tumors without the production of an arteriovenous fistula does sometimes occur, with the production of a chain of symptoms and signs not to be distinguished clinically from the arteriovenous aneurysm group. Shennan[1] reviews five such cases.

Prognosis is very grave. In sixty-two instances of arteriovenous aneurysm between the aorta and superior vena cava or left innominate vein 88 per cent have died in less than two months following the onset of symptoms.

SUMMARY

1. A case of aortic aneurysm rupturing into the superior vena cava is described, including clinical and anatomical data.

2. Similar cases in the literature are discussed.

3. The etiology, incidence, symptoms, signs and prognosis are considered.

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I. AN EXPERIMENTAL STUDY OF THE EXTRACARDIAL NERVES*

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INTRODUCTION

THE chilling of the heart which results from exposure when the thorax is opened is known to affect the activity of the accelerator nerves.[1] It was therefore considered of interest to study the accelerator nerves when the body temperature is maintained at the normal level. There have been studies of the accelerator nerves by Friedenthal,[2] De la Camp,[3] Jonnesco and Ionescu,[4] Rothberger,[5] Danielopolu and Marcu,[6] and others. Jonnesco and Ionescu concluded their study with the statement that the accelerator nerves are of no importance to the life of the heart ("die Acceleratoren keine lebenswichtigen Nerven sind"). Rothberger has expressed a contrary opinion. That a healthy dog can live after section of the vagi and removal of the stellate ganglia has been demonstrated by Friedenthal and De la Camp. The solution to the question regarding the accelerator nerves in their relation to the surgical treatment of angina pectoris is probably better approached by searching for the degree to which accelerator nerve section interferes with the functioning of the heart when abnormal conditions of circulation are present, and the determination of the extent to which the accelerator nerves are a source of reserve or support for a heart that is on the verge of failure. The present investigation has attempted to approach the accelerator nerve mechanism from this viewpoint, by determining its relation to the heart under various abnormal conditions of rhythm and injury. The effect of coronary ligature has also been included. A preliminary study of the effect of accelerator nerve section upon the intact and uninjured heart was first made.

THE EFFECT OF ACCELERATOR NERVE SECTION UPON THE INTACT HEART

Method.—Adult dogs were tested, with an average weight of 13 kilos (variation 6 to 20 kilos). Most of them were narcotized with chloretone. Artificial maintenance of the body temperature was obtained by means of an electric heating apparatus. The temperature variation was usually not greater than 1° C. above or below the temperature present when the experiment was begun (whereas uncontrolled a fall of from 4° to 7° occurs). The preparation of the animals included tracheotomy and artificial respiration, bilateral vagus section and the opening of the thorax. The time for surgical preparation usually occupied between fifteen and twenty minutes. Where stimulation of the accelerator nerves was not included, the ganglia stellata were removed. Changes in the heart were recorded by observation of changes in the character of the beating and the heart rate, and axial electrocardiograms (R.A.-L.L., with copper, needle-shaped electrodes). The

*From the Laboratory of Physiology of the Faculty of Medicine, Paris.

observations were made at five minute intervals for from twenty to sixty minutes before accelerator nerve section. The effect of the nerve section was followed over periods of time up to three hours after. Blood pressure changes when followed were recorded from the left carotid artery with a mercury manometer.

RESULTS

Effect on Heart Rate.—Of the 49 animals tested, 32 (65 per cent) presented no alteration in the heart rate following accelerator nerve section. In 16 (33 per cent) a fall in the rate occurred. In 11 of these 16 the fall in the rate was less than 20 beats per minute (10 per cent), and in the remaining 5 the fall in rate was more than 20 beats per minute (13 to 36 per cent). (Table I.) In 5 of 49 animals (10 per cent), therefore, a significant fall in the heart rate accompanied the nerve section.

TABLE I

	RATE DROP			
BEFORE	IMMEDIATELY AFTER	1 HOUR AFTER	TOTAL FALL	PER CENT FALL
158	142	136	*22*	14
146		136	10	
150		139	11	
146		139	7	
120		108	12	
136	122	100	*36*	26
158	130	100	*58*	36
154	150	134	*20*	13
160		152	8	
140		130	10	
166		158	8	
148		136	12	
150		133	17	
160		146	14	
156	130	126	*30*	19

In one animal (2 per cent) death followed. Immediately after the accelerator nerve section, the heart rate fell from 120 to 100 and this was accompanied by a visible increase in the size of the heart and a decrease in the strength of its contractions. The heart rate continued to decline until death ensued ten minutes after the nerve section. The constant heart rate during the period before the accelerator nerve section suggested that the relation of the accelerator nerve section to the heart failure in this instance might have been causal.

In the group of animals in which a decrease in heart rate occurred a considerable part of the total fall in the rate followed immediately upon the accelerator nerve section (Table I). The drop in the rate following the section of the right nerve was always much greater than that following the section of the left nerve, irrespective of which nerve was first sectioned.

The Vagus Nerve.—No relation existed between the response of the heart to the stimulation of its right vagus nerve and the degree to

which the accelerator nerve section affected the heart. In the single instance in which death occurred after accelerator nerve section, right vagus nerve stimulation induced complete stoppage of the heart the entire time of stimulation with no "escape," but this high degree of vagus sensitivity was frequently observed among the group in which accelerator nerve section caused no observable alteration of the heartbeat.

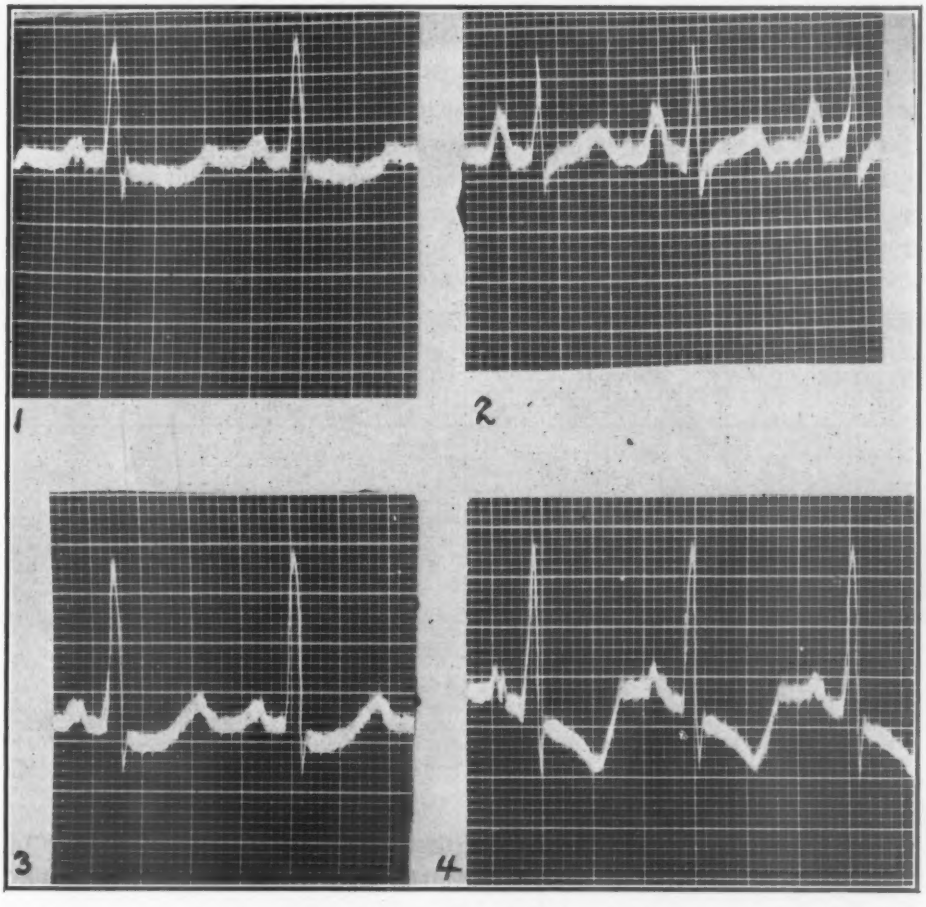

Fig. 1.—The effect of stimulation of the right accelerator nerve—axial electrocardiograms. Time in fiftieth seconds. 1, normal; 2, after stimulation of the right accelerator nerve; the reverse of the usual effect. 3, Normal, the line of the lead has been rotated counterclockwise through 45°; 4, after stimulation of the right accelerator nerve; the characteristic effect upon the T is present. ST fusion (beginning of the T before the complete ascent of S) is also present.

The Electrocardiogram.—No significant or constant alteration in the form of the curves was observed to follow the accelerator nerve section. This agrees with the findings reported by Jonnesco and Ionescu[4] but does not accord with those of Danielopolu and Marcu,[6] who have reported significant changes in the form of the electrocardiogram after removal of the stellate ganglia.

Accelerator Nerve Stimulation.—The effects of right and left accelerator nerve stimulation were like those which have been reported,[1]

the stimulation of the right accelerator nerve inducing a decrease in the height of the T-wave, or negativity of the T-wave; and the stimulation of the left accelerator nerve the reverse, i.e., positivity of the T-wave. No instances occurred in which the left accelerator nerve stimulation induced the RT fusion.[7, 1] On the other hand many instances of ST fusion appeared following stimulation of the right accelerator nerve. (Fig. 3, Sections 3 and 4.) This, however, only appeared when the electrocardiogram preceding the stimulation presented a negative RT interval. In those instances in which right accelerator stimulation did not cause negativity of the T-wave and left accelerator nerve stimulation positivity of the T-wave, the effects described by Rothberger and Winterberg[7] appeared.

In two instances the effect of stimulation of the right accelerator nerve was to elevate the T-wave and of the left accelerator nerve to depress the T-wave, i.e., the reverse of the usual effect. In these, an

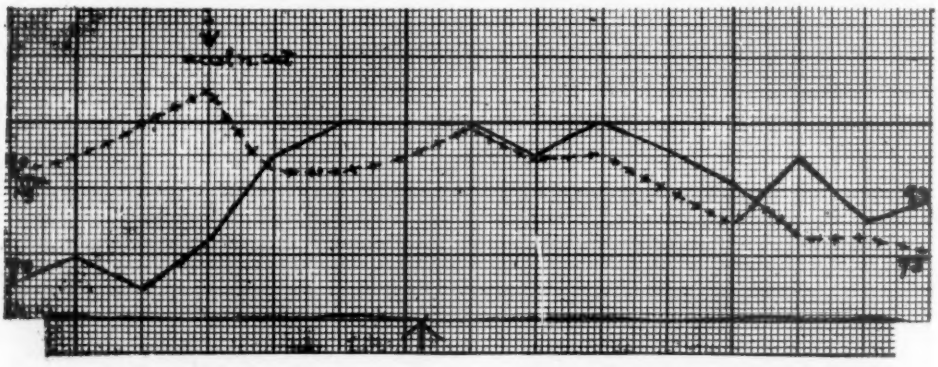

Fig. 2.—Curves of the blood pressure of two dogs in which the heart rate was constant. In one of them the accelerator nerves were cut at the point indicated by the arrow (curve of +++). The nerve section causes a slight fall in the blood pressure when the heart is unchanged. Heart rate (curve of +++) 167-171; Heart rate (curve of ——) 133-137. (Abscissae, 1 mm. = 1 mm. of mercury pressure; ordinates, 1 mm. = 1 minute.)

alteration of the line of the leading across the heart (the direction of the leading was unchanged) presented the usual effect. (Fig. 1.) Further studies upon this have been made.

Blood Pressure.—A fall in the height of the systolic blood pressure which was proportionate to the fall in the heart rate followed the accelerator nerve section. However, in instances in which there was no decline in the heart rate following accelerator nerve section, a slight fall in the height of the systolic blood pressure immediately followed the accelerator nerve section and a slight decline continued over the period of observation following the nerve section. This was not the case in the control animals, systolic blood pressure either mounting or remaining constant. (Fig. 2.) This suggests that the accelerator nerve section produced some effect of decreased force of contraction when the conditions of heart rate were unchanged.

Accelerator Nerve Section and Heart Injury.—That accelerator nerve section might be followed by serious cardiac changes leading to death of the heart was suggested by some of the results. The age of the animal is not a factor in this, because many of the dogs sustaining accelerator nerve section without a change in the heart rate were old animals with thickened and tortuously beating carotid arteries. In the dog it was observed that vagus sensitivity was more pronounced in the older animals, which corresponds to the increase in vagus activity which accompanies advancing age in the human. Most of the dogs presenting a vagus reaction so intense as to cause stoppage the entire time of stimulation were old dogs.

The effect of accelerator nerve section after the heart was injured in a great variety of ways was tested and no condition was met such that accelerator nerve section constantly resulted in circulatory failure and death, although in some (particularly with types of injury which depressed the heart muscle) the effect of the accelerator nerve section was increased. The injury to the heart was obtained in the following ways: toxic quantities of chloretone, ether, or chloroform and sundry other drugs were also tested (magnesium and sodium sulphate, potassium chloride, alcohol, bile salts, yohimbine, lactic acid, atropine, pilocarpine, amyl nitrite, digitalis). The forms of mechanical injury were precipitation of the muscle substance with alcohol injection, crushing or cutting of the muscle, mechanical interference with the heartbeat by filling the pericardium with large amounts of saline and partial ligation of the aorta, and the production of valve insufficiency by ripping or cutting the tricuspid, aortic, and bicuspid valves. Great lowering of the blood pressure and excessive hemorrhage were also tested.

Effect of Accelerator Nerve Section Upon Nodal Rhythm.—When nodal rhythm was induced by the ligation of the blood supply to the S.A. node[8] no significant effect upon the heart occurred as a result of accelerator nerve section. The results paralleled those obtained when the normal sinus rhythm was present. (Table II.) Likewise the greater drop in the rate always accompanied section of the right accelerator nerve.

TABLE II

NODAL RHYTHM

DOG NO.	RATE BEFORE	RATE AFTER	I HOUR LATER	PER CENT DROP	AFTER SECT. ACCEL. N.	I HOUR LATER	PER CENT DROP	
15	150	114	114	24	accel. n. sect. before nodal rhy. induced			
17	150	110	110	27	accel. n. sect. before nodal rhy. induced			
10	150	69	69	54	accel. n. sect. before nodal rhy. induced			
33	167	93		44	93	91		
31	154	73		53	61	58	16	
36	139	65		54	53	47	18	
34	142	93		34	73	68	21	
37	150	71		52	68	66	4	

SUMMARY

1. The effect of accelerator nerve section in animals with intact hearts was insignificant in the vast majority of the animals tested (43 of 49 dogs) although the remaining number showed considerable effects from the section, and the section probably caused death in one of them.

2. The relation of the right vagus nerve, the electrocardiogram and the blood pressure to the effects of accelerator nerve section were studied.

3. The effect of accelerator nerve section in the presence of numerous types of cardiac injury and nodal rhythm was studied and was not found to be significantly greater than when the heart was uninjured.

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II. AN EXPERIMENTAL STUDY OF THE EXTRACARDIAL NERVES*

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INTRODUCTION

THE effect of accelerator nerve section in the presence of various types of cardiac injury is not great when the S-A node controls the heart's rhythm,[1] and this is also the case when A-V rhythm is present. This study is concerned with the effect of accelerator nerve section in the presence of block induced above and below the A-V border. Accelerator nerve action in heart-block has been studied by Hering,[2] Cullis and Tribe,[3] Daly and Starling,[4] and others. These studies, however, are not directly concerned with the effects of the accelerator nerve section upon the heart, and an artificial circulation was maintained (the perfused heart being used).

METHOD

Dogs of medium weight, under chloretone narcosis, artificial respiration, vagus section, opened chest, artificially maintained temperature, and axial electrocardiographic leading, were utilized. Complete block above the A-V border was induced by cutting the interauricular septum close to its ventricular margin or precipitation of the tissues in that area by the injection of 95 per cent alcohol. There were nine dogs with this type of block. The injection or the position of the cut could be recognized post-mortem, and its relation to the ventricle determined. Since the injury was above the A-V border, these hearts may be regarded as suffering functional separation of the auricles and ventricles† with a small portion of the auricles belonging to the interauricular septum, which was probably part of the A-V node, remaining in continuity with the ventricles.

Complete block below the A-V border was induced in the same fashion at the mainstem of the bundle or section of its principal divisions upon the ventricular septum. The heart was not greatly disturbed by the mechanical injury caused in producing the block unless the injuries were severe. Rothberger[5] has commented upon the extensive injury of this sort that the heart will endure without serious impairment of its function. In some of these hearts the block was induced after the section of the accelerator nerves and in others the accelerator nerves were sectioned after the block.

RESULTS

Heart-Block in the Auricle.—In Table I is given the heart rate before and after the induction of the block.

The rate of the auricle after the block was induced was not significantly altered. There was no relation between the heart rate previous to the block and the rate at which the ventricles beat after the block was established.

*From the Laboratory of Physiology of the Faculty of Medicine, Paris.

†The A-V bundle constitutes the only functional connection between the auricle and the ventricles in the dog.[12]

TABLE I

DOG NO.	RATE BEFORE	RATE OF A.	RATE OF V.
28	137	137	45
32	150	158	35
35	154	150	78
40	154	167	67
41	124	138	74
61	130	130	45
157	180	178	64
158	130	130	36

Accelerator Nerve Section.—Accelerator nerve section induced a variable amount of decline in the heart rate which mainly affected the auricle but induced no further changes in the character of the heart-beat nor the electrocardiogram over periods of observation the longest of which was two hours. This is similar to the effect of section of the accelerator nerves in the intact heart. The greatest effect always followed the section of the right accelerator nerve as was the case with normal sinus rhythm and nodal rhythm. (Table II and Fig. 1.)

TABLE II

DOG	RATE BEFORE	R. ACCEL. N. CUT.			L. ACCEL. N. CUT.		
	142	104		104	100		93
28	—	—	20 min. later	—	—	40 min. later	—
	44	45		39	38		38
	136	90		92	93		100
35	—	—	20 min. later	—	—	30 min. later	—
	78	72		67	61		58
		L. ACCEL. N. CUT.			R. ACCEL. N. CUT.		
	167	167		150	120		106
40	—	—	40 min. later	—	—	20 min. later	—
	50	52		64	65		62
	148	148		154	102		75
41	—	—	20 min. later	—	—	60 min. later	—
	65	65		61	60		44

Effect of accelerator nerve section upon heart-block in the auricle.
Rate of auricle is above the ——, and that of the ventricle below.

The effect of the accelerator nerve section upon the auricles and ventricles was not proportionate and was in no way related. The greater part of the decline in the rate after the accelerator nerve section, in the case of the auricles, was an effect which immediately followed the nerve section, whereas the decline in ventricular rate when it occurred was gradual (Fig. 1 and Table II). These changes in the ventricular rate did not as a rule significantly exceed the gradual decline which is common with experimental heart-block, occurring without accelerator nerve section. In one instance, however, it was marked and caused death, the rate declining in one hour from 130/45 to 110/14, although the accelerator nerves were intact.

Heart-Block in the Ventricle: Heart-Block After Accelerator Nerve Section.—Block was induced in from thirty to ninety minutes after the accelerator nerve section, and in from five to ten minutes after the onset of the independent rhythm of the ventricle asphyxial gasping movements (indicating cerebral anemia from circulatory failure) appeared. A decrease in the strength of the contractions accompanied this and progressed until the ventricular contractions became extremely feeble before the heart stopped beating, but a decrease in the ventricular rate did not constantly accompany this and in several instances the ventricular rate had not altered when circulatory failure occurred. This

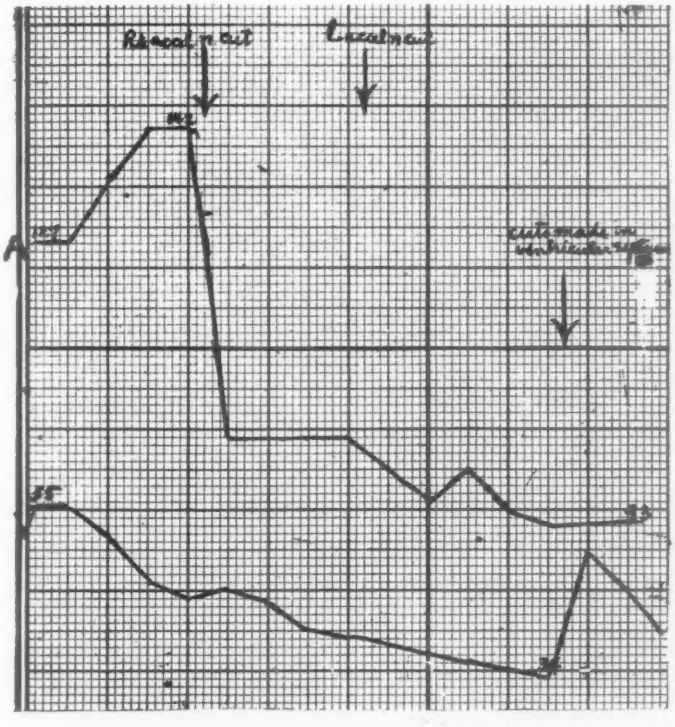

Fig. 1.—Plotted rates of auricle (A) and ventricle (V) in a dog with heart-block in the auricle. The base line is not shown, and the curves are moved closer together. Ordinates 1 mm = 1 minute; abscissae 1 mm. = 1 heartbeat per minute. The arrows indicate, successively, the points at which section of the right accelerator nerve, left accelerator nerve, and an injury to the septum were made.

rapid circulatory failure did not occur whenever a recovery of the A-V conduction was impending (evidenced by its later appearance) or whenever partial heart-block was present.

It is not probable that the mechanical insult offered to the heart by the induction of the heart-block was the cause of the circulatory failure, inasmuch as cutting injury to the heart muscle increased the ventricular rate and muscle tone (Fig. 1) and severe cutting injuries to the heart muscle were shortly followed by the onset of ventricular fibrillation, which was the case whether or not block was present or the accelerator nerves intact or sectioned.

In 7 of the 15 animals the effect of accelerator nerve stimulation was tested and in 4 of them it was ineffective in preventing the onset of the rapid circulatory failure (diastolic heart death). In these there was no accelerator nerve stimulation until the asphyxial gasping, which indicated the presence of circulatory failure, had appeared. In the other 3 animals the accelerator nerves were stimulated directly after block was induced. In these the accelerator nerve stimulation prevented the onset of the diastolic heart death and the circulation was maintained. In 5 animals of the next group (accelerator nerves sectioned after block induced) accelerator nerve stimulation likewise maintained the circulation during the period of the experiment.

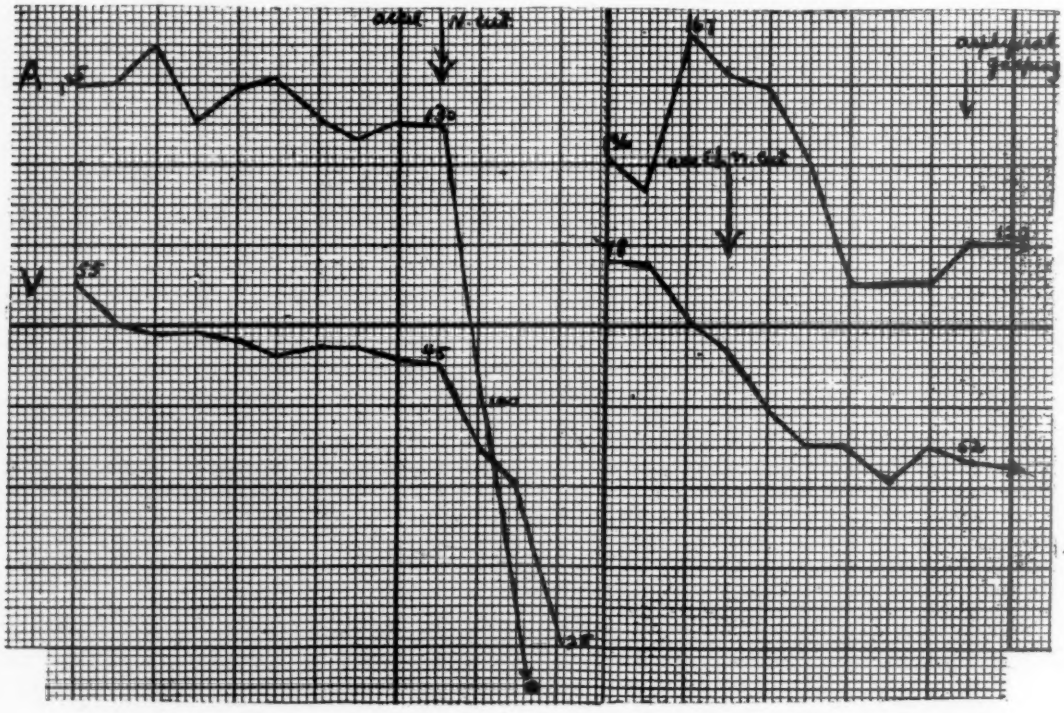

Fig. 2.—Plotted rates of auricle (A) and ventricle (V) in two dogs with heart-block in the ventricle. The base line is not shown, and the curves are moved closer together. Ordinates 1 mm. = 2 minutes; abscissae 1 mm. = 1 heartbeat per minute.

Accelerator Nerve Section After Heart-Block.—Complete heart-block was induced in 22 dogs in which the accelerator nerves were intact. In 13 of the dogs the effect of accelerator nerve section was tested. From thirty to ninety minutes intervened between the induction of the block and the nerve section. In all of them circulatory failure and diastolic heart death occurred at a variable interval (twenty-five to fifty minutes) after the accelerator nerve section.

Effect Upon the Heart Rate and Rhythm.—The accelerator nerve section caused an immediate fall in the rate of the auricles (Fig. 2), and the effect of section of the right nerve was always considerably

greater than the effect of the section of the left nerve. The auricular rate then slowly declined until it was about 100 per minute and the auricle stopped beating as a rule just before the onset of the signs of circulatory failure (asphyxial gasping). Phasic variation in the rate of the auricle frequently appeared during the course of the decline in the rate, the electrocardiogram of which most often revealed no alterations in the form of the P-wave. Shortly before standstill great irregularity in the rhythm of the auricle was frequent. Here, too, the electrocardiogram presented no change in the form of the P-wave, suggesting that it was the effect of a sinus block or a failure of the rhythm of the sinus itself.

No immediate decline in the rate of the ventricles followed the accelerator nerve section, as was the case with the auricles. In some cases only a very little decline in the rate had occurred when the signs of circulatory failure appeared (Fig. 2). The most constant effect upon the ventricles was a decline in the visible tone of the ventricular muscle and the strength of its contraction. That the changes in its rate were unrelated to the accelerator nerve section was also suggested by the occurrence of instances with great fall in the ventricular rate in the presence of intact accelerator nerves, with little apparent alteration in the muscle tone.

In each instance in which this type of diastolic death did not occur following the accelerator nerve section, evidence appeared to indicate that complete block, the location of which was in the ventricle, was not present. For example:

In Dog 26 the block appeared to be complete during seventy minutes of observation after which the accelerator nerves were sectioned. The recovery of the normal sinus rhythm occurred ten minutes later. Over the ensuing forty-five minutes no observable changes occurred except a decline in the heart rate from 158 to 130. At this time heart-block was reestablished and diastolic death occurred ten minutes later.

In Dog 73 the block was complete except for an occasional impulse passing from the auricle to the ventricle. During a period of observation of forty minutes this did not occur more often than once a minute. Occasionally 2 or 3 consecutive beats passed from the auricle to the ventricle. Seventy minutes after accelerator nerve section the heart function was the same and the circulation unimpaired. The section of the left bundle was repeated. The diastolic death appeared fifteen minutes later.

In Dog 147 the block appeared to be complete during sixty minutes observation before the accelerator nerves were sectioned. One hour after this the circulation was unimpaired. Adrenalin, 0.2 c.c., intravenously, a procedure which invariably resulted in the immediate onset of ventricular fibrillation whenever the block was complete,

caused the heart rate to rise to 176 and the electrocardiogram showed a 1:1 rhythm during this period of tachycardia (Fig. 3). After the effect of the adrenalin had passed, the heartbeat again resumed the appearance of complete block. Repetition of the procedure produced the same results.

There were 4 animals in which the induction of the complete block resulted in circulatory failure and death, although the accelerator

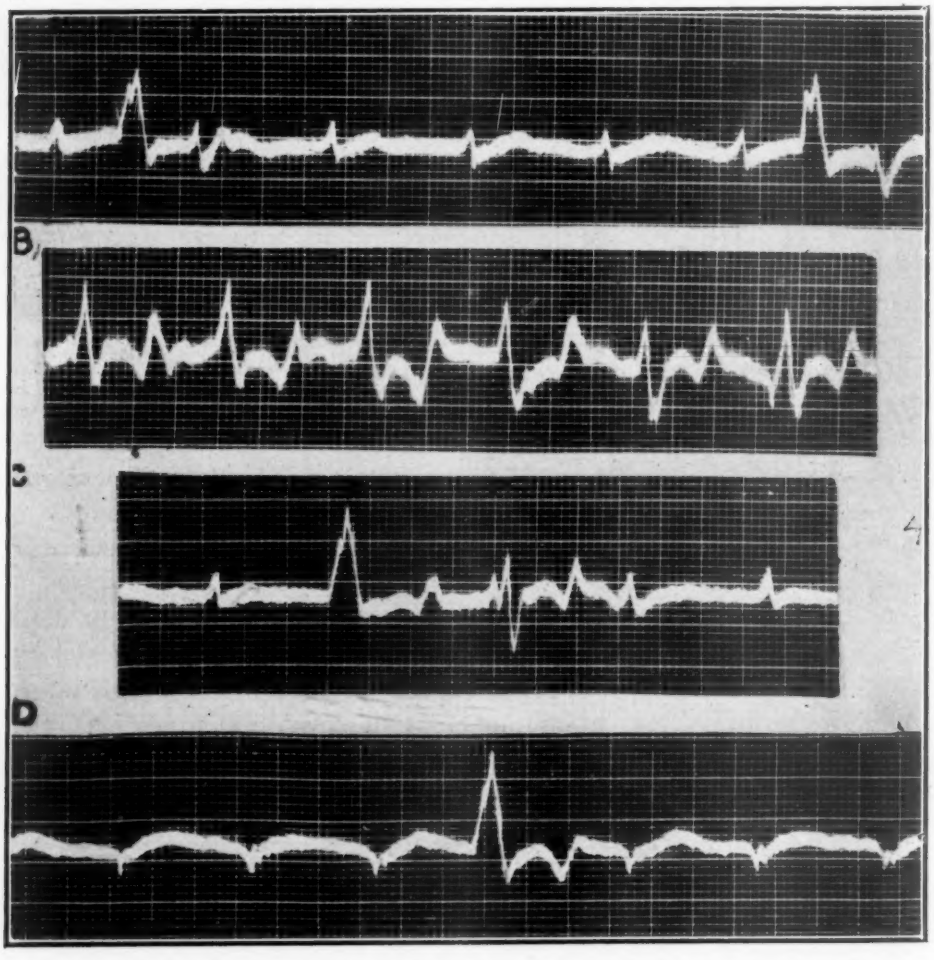

Fig. 3.—Dog. 147. Axial leading, time in fiftieth seconds. *A.* One hour after accelerator nerve section. The block appeared complete. *B.* After 0.2 c.c. adrenalin intravenously. Although P-waves are not clearly discernible, the form and regularity of the tracing indicate that the ventricle was following supraventricular impulses. *C.* Three minutes later. Heart-block is returning. What seems to be a response to an impulse coming from the auricles is present. *D.* The heart-block again appeared complete.

nerves were intact. In 2 of them the results were indistinguishable from those obtained when the accelerator nerves were sectioned. The death occurred in ten and twenty minutes respectively. In these animals there was difficulty in inducing the ventricle to beat after block was established, and following a short rhythm of development, the

ventricular contractions declined in strength until circulatory failure appeared. In one of the remaining two circulatory failure appeared thirty-five minutes after the block as a result of the decline in heart rate (from 42 to 14), with no apparent alteration of the muscle tone and strength of contraction. An instance like this appeared among the group with block in the auricle. In the other, circulatory failure appeared after thirty minutes during which time complete block with recovery and reinduction of the block occurred 7 times. In all of the animals excepting three the injuries to the heart were entirely confined to the ventricle. In the three exceptions the block was induced by alcohol injection and the coagulation area was large and was confined to the interauricular septum, but extended along its base to the upper margin of the septum of the ventricle. A comparison of the post-mortem findings with the effect of accelerator nerve

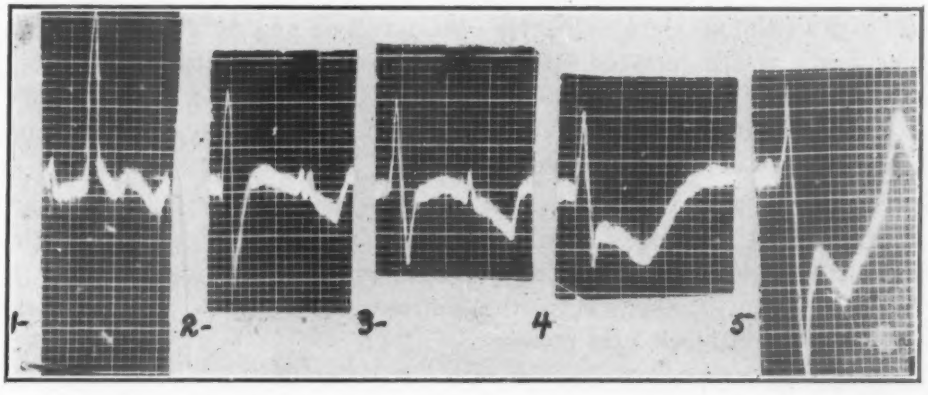

Fig. 4.—Axial electrocardiograms. Time in fiftieth seconds. One beat from each electrocardiogram is arranged on the same isoelectric level. (1) The form of the QRST with the normal sinus rhythm present; (2) complete heart-block; (3) thirty-five minutes after removal of the stellate ganglia and just after asphyxial gasping had appeared; (4) seven minutes later; (5) again seven minutes later.

section indicated that the level of the heart-block bore no relation to the effect upon the heart of the nerve section except in so far as it permitted auricular tissue to remain in functional continuity with the ventricles.

Electrocardiogram.—The electrocardiogram showed no changes in form following the accelerator nerve section until circulatory failure appeared. The changes which then appeared were a progressive deepening of the T-wave and the appearance of the ST fusion. (Fig. 4.) This was followed by the changes which are known to be associated with the dying heart, viz., great spreading and notching of the QRS complex, bizarre alterations in the form of the T-wave, and huge, broad monophasic curves.

COMMENT

When complete block of the type which severed the functional association of the auricular tissues with the ventricles was produced,

circulatory failure principally due to progressive loss of the muscle tone and strength of contraction resulted twenty-five to fifty minutes after the accelerator nerves were sectioned. The relation of the accelerator nerves to this was also indicated by the effect of accelerator nerve stimulation. On the other hand, the relation of the upper cardiac chambers to this may be inferred by the fact that comparatively infrequent impulses from the auricle were sufficient to prevent the onset of the circulatory failure, and by the result when complete heart-block was produced in a fashion which left a piece of auricular tissue in functional association with the automatically beating ventricle, although the appearance of the heart and its rate of beating in the two types of heart-block was the same.

It is probable, therefore, that there were two sources for this inotropic support of the ventricles, without the activity of one or the other of which circulatory failure ensued. One of these was the tonic activity of the accelerator nerves—an extrinsic and nervous influence. The other was associated with the impulse to contraction which descends from the upper chambers through the bundle of His and was intrinsic in character. This intrinsic action might be due to a mechanical, nervous or chemical mechanism.

Since mechanical irritation can raise the muscle tonus, it could be assumed that it was of this nature, i.e., an effect of the rhythmic mechanical stimulation of the ventricle by its own contraction. It did not, however, occur from the contractions of the ventricle when complete heart-block was present.

If it was nervous it was not the effect of section of accelerator nerve fibers passing to the ventricles by way of the bundle, and the assumption is necessary that a local reflex from auricle to ventricle was broken, the paths for which are located in the bundle of His. It is conceivable, however, that this intrinsic nervous pathway between the auricles and ventricles, although contained in the bundle, is independent of the excitation which descends the bundle and which is probably a muscle contraction.[6]

The remaining possibility is that it was chemical in nature. The findings of Demoor[7] and Haberlandt[8] suggest this. However, this action cannot be the effect of a true hormone, since the substance, if it existed, was not liberated into the blood stream. Otherwise the removal of the accelerator nerve tonus would not have been followed by circulatory failure. If it is chemical, it was distributed by an intracardiac channel which must be the bundle of His, and this does not seem probable. Moreover, a direct test of the question by the use of Ringer's solution and 40 per cent alcohol solution extracts from the specific tissues (S-A and A-V nodes and the bundle of His) of the fresh ox, sheep, and dog heart was made and was without effect.

Anrep and Segall[9] have pointed out the reflex nature of the dilator

action of the accelerator nerve tonus upon the coronary vessels of the heart of the dog and its function in elevating the volume of coronary flow. On the other hand, when perfused hearts are used to study accelerator nerve action in heart-block[2, 3, 4] this peculiar effect of accelerator nerve section is not met. This suggests that it was due to a critical condition of the coronary circulation in which the abolition of the reflex capillary dilatation afforded by the accelerator nerve mechanism caused an insufficiency of the coronary circulation which in turn induced the loss of the muscle tone. Although diastolic blood pressure determines the coronary flow,[10, 11] the source of the heart failure was intracardiac and dependent upon the functional separation of the auricle from the ventricle, since the same phenomenon could not be produced by a great lowering of the blood pressure and it did not appear when the point of the block was in the auricle.

If this be the case it is probable that the nature of the action exerted by the auricle through the bundle of His is the same as that of the accelerator nerves, it maintains a capillary coronary dilatation.

It is not probable that the ventricles of the human heart when complete heart-block is present depend upon the accelerator mechanism to the extent which was here exhibited, inasmuch as the conditions of the experiments (anesthesia and the excessive surgical preparation involved) from the viewpoint of a clinical comparison are exceptional. It suggests, however, another aspect of the function of the accelerator nerves.

SUMMARY

1. The effect of accelerator nerve section upon heart-block was found to be insignificant when very high grades of partial block were present or when the point of the block was in the auricle, but when the block was complete and when it functionally isolated the ventricles from auricular tissues circulatory failure occurred.

2. The changes associated with the circulatory failure are described.

3. The presence of an intrinsic cardiac reflex is suggested.

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THE SO-CALLED SUPERNORMAL RECOVERY PHASE OF CONDUCTION IN HEART MUSCLE*

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THE idea of a supernormal recovery phase in heart muscle owes its origin to the work of Adrian and Keith Lucas,[1] and Adrian.[2] These observers studied recovery curves of nerve, skeletal, and heart muscle after an initial stimulus and response by testing at varying intervals and with varying strengths of stimuli. They found that when these tissues were bathed in relatively acid fluids, an overswing of the recovery curve could be obtained. Thus during a brief time-interval in the recovery period, stimuli too weak to elicit a response from resting tissues were effective. After this so-called supernormal phase, the threshold returned to the resting level. No satisfactory explanation for these observations is forthcoming, nor perhaps is any to be expected until the physiological properties of nerve and muscle are better understood. The tissue response is possibly related to the much better known "Treppe" or staircase phenomenon.

Lewis and Master[3] in two clinical cases and later Ashman and Herrmann,[4] also in two clinical cases, employed the conception of a supernormal phase of conduction in heart muscle to account for the transmission of the excitatory process from auricles to ventricles during certain sharply delimited periods, when impulses falling either earlier or later failed to be transmitted.

The interpretations of Ashman and Herrmann were fortified by experiments made by Ashman[5] on turtle heart muscle which he believed to display a supernormal phase. Lewis and Master, however, state that they did not discover any evidence of a supernormal phase in their experiments on conduction made in mammalian heart muscle.

The case to be reported here appears to exhibit a mechanism somewhat similar to that of Lewis and Master's Case 1 which displays most clearly the type of transmission attributed to a supernormal phase of conduction.

REPORT OF CASE

K, a man fifty-six years old, a Russian Jewish tailor, was first seen in the Cardiovascular Clinic of the University Hospital, May 7, 1921. His chief complaint at that time was indigestion, but on examination he was found to have moderate cardiac enlargement, evidences of slight aortic regurgitation, and auricular fibrillation. In spite of the fact that he had received no digitalis the ventricular

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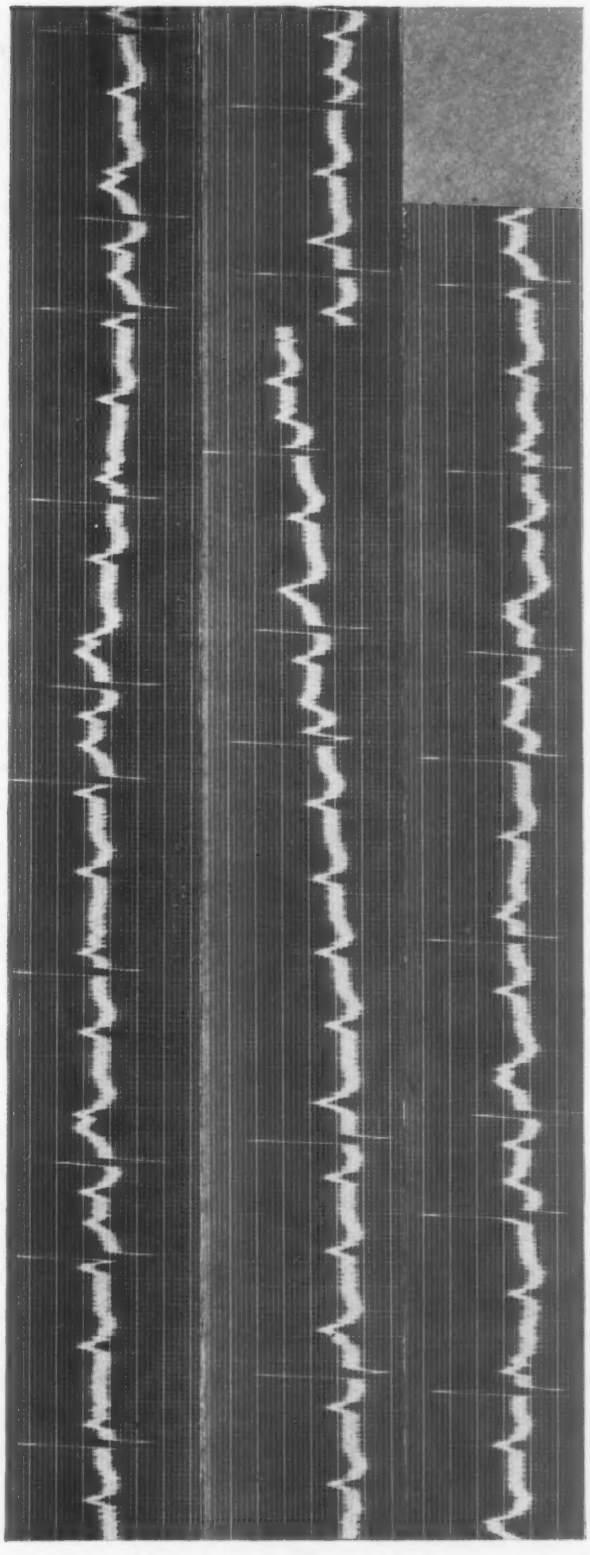

Fig. 1.—Continuous tracing, Lead II, all P-waves whose beginning falls in the time interval 0.45-0.74 second after the preceding QRS complex are transmitted, but otherwise dissociation is complete. The range of P-R intervals is 0.24-0.28 second.

rate varied between 65 and 75. Studies of the gastro-intestinal tract proved negative but gastric symptoms persisted, nor did they clear up after several weeks of rest. Sinus rhythm was then restored by a few doses of quinidine. Following the return of normal rhythm the digestive symptoms disappeared and the patient was able to return to his work as a tailor, and continued working two years. During this time he reported for observation frequently and numerous electrocardiograms were made. All showed a prolonged P-R interval varying from 0.24 to 0.30 second—a finding which probably accounted for the fact that the ventricular rate had been no more rapid during auricular fibrillation. Finally the development of symptoms of circulatory inadequacy led one of the clinic staff to prescribe digitalis. This was quickly followed by complete dissociation. There were periods of cessation of ventricular action lasting from three to four seconds, accompanied by momentary attacks of vertigo and clouding of consciousness. Sequential beating could be readily restored by the intramuscular injection of atropine sulphate, gr. 1/50, although P-R intervals always remained prolonged. Dissociation recurred in a few hours after atropine injection. During the last

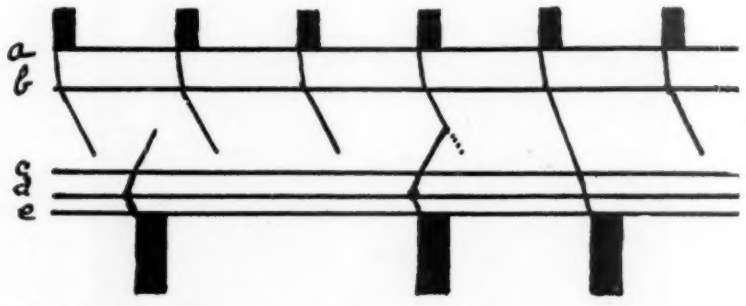

Fig. 2.—A diagrammatic representation of how a longer rest period in a part of the critical area of conduction in the junctional tissues (b-c) might be brought about, thus favoring the transmission of the next beat. The impulses associated with the fourth auricular and the second ventricular beats are represented as traveling in such a manner as to meet and cause block of the descending impulse at a higher level than usual. The longer rest period resulting therefrom is represented by the horizontally lined area.

few days of life dissociation could not be abolished by atropine. The patient died suddenly, August 15, 1924, during a crisis of hypertension.

Four times during the course of our studies tracings were obtained showing the type of ventricular irregularity present in Fig. 1. Twice under our observation it continued for three hours and may have persisted much longer. The irregularity was due to the fact that impulses were capable of being transmitted during a brief period following ventricular systole. Measurement of tracings showed that when the beginning of a P-wave fell in the period 0.45-0.74 second after the beginning of the QRS complex, transmission to the ventricles resulted, but that it did not occur during any other period of the cycle. On the four occasions that the irregularity was recorded, almost every auricular excitation falling in the 0.45-0.74 second interval following a QRS complex was transmitted, whereas no auricular excitations falling outside this interval were transmitted.

COMMENT

The fact that our case of otherwise complete dissociation exhibits effective transmission of the excitatory process from auricles to ventricles during a period related to the preceding idioventricular beat indicates that the latter has been in some way responsible for the transient recovery in conduction. There are at least three possible explanations applicable to our case for this recovery: namely, (1) supernormal phase of recovery, (2) prolongation of the rest period in the area of block, and (3) transient improvement of the nutrition in the area of block due to ventricular systole and increased blood flow.

1. It must be admitted that if we are permitted to assume the presence of a supernormal recovery phase of conduction as this conception has been developed by Lewis and Master, and Ashman and Herrmann, the mechanism of recovery exhibited in our case as well as in the cases reported by these observers may be logically accounted for. In our case with the regular auricular rate we must assume that the idioventricular excitatory process not only descends to the ventricles but also spreads in the retrograde direction penetrating for some distance into the critical area of block. During the recovery period in the area of block, following the retrograde excitation, a supernormal phase occurs. If an excitation from the auricles reaches the critical area of block during the supernormal recovery phase, transmission through this area to the ventricles takes place.

In the present state of our knowledge, there is one serious objection to this hypothesis. We have no proof that mammalian heart muscle is capable of a supernormal phase. It has been discovered only in cold-blooded heart muscle under highly artificial experimental conditions. It would, therefore, seem desirable to account for our observations, if possible, on better established physiological principles.

2. It is well known that when the ability to transmit impulses is impaired the length of rest periods may have a very important effect on this function. When the function is in a highly critical state, even slight differences in rest periods may be of importance. In Fig. 2 in which the incidence of auricular and ventricular beats, including a transmitted beat is diagramed, it is shown how an impulse arising from the idioventricular pacemaker may penetrate part of the area of block and meet an auricular impulse descending from above. Under these conditions the further descent of the auricular impulse is stopped and the tissue which it might otherwise have traversed obtains a longer rest period before the next impulse descends. Thus it is conceivable that sufficient recovery may occur to permit transmission through the critical area. An analysis of all our tracings shows that such a mechanism might have been operative in connection with every recorded instance of transmitted beats.

It would be difficult from the published tracings to rule out this mechanism as operative in Ashman and Herrmann's Case II. It might also be a factor in association with vagus changes in their Case I. It does not, however, seem to be applicable to Lewis and Master's Case I in which the transmission intervals are brief.

3. The third possible explanation for recovery of conduction concerns variations in blood flow during the ventricular cycle. Unfortunately we possess little satisfactory experimental data for blood flow variations during the cardiac cycle and naturally no clinical data. According to Anrep, Cruickshank, Downing and Rau,[6] coronary flow is practically at a standstill during ventricular systole but begins after aortic closure and tends to increase up to the time of the next ventricular systole. These observers, however, were working with healthy coronary vessels and rapid ventricular rates. If the coronary vascular apparatus is diseased, it is not unreasonable to suppose that its greatest circulation might occur during that part of the diastole in which arterial pressure is greatest, namely, shortly after aortic closure or the beginning of diastole. Such a consideration would have special force in the presence of aortic regurgitation and very slow ventricular rate, such as our patient showed, since the pressure fell during diastole to a very low level.

Electrocardiograms during complete heart-block give no indication as to when aortic closure occurs, since the point of subsidence of the T-wave does not correspond to it, the latter usually occurring later. Thus, in our case it is possible, even probable, that coronary circulation reached its maximum flow before subsidence of the T-wave.

If these considerations warrant the assumption in our case that coronary flow is most active during early diastole, it is still necessary to account for transient recovery in conduction. Available evidence would seem to indicate that anoxemia and a shift in reaction toward the acid side, conditions which tend to occur in cells when the circulation is sluggish, markedly depress conduction. On the other hand, there is no data bearing on how rapidly recovery may occur. The experiments of Hartridge and Roughton[7] show that *in vitro* chemical changes through red cell membranes occur with startling rapidity. This observation suggests that they also occur rapidly *in vivo;* therefore, if chemical and functional changes run parallel, there would be ample time for recovery in function.

Thus it is possible to construct an hypothesis based on the two assumptions of (1) increased coronary blood flow during early ventricular diastole and (2) associated improvement in the function of conduction, which will satisfactorily account for all the clinical phenomena attributed to a supernormal phase in conduction.

The occurrence of the shortest transmission intervals at the beginning of the period of conduction, a point stressed by Lewis and

Master, and by Ashman and Herrmann as in favor of the supernormal phase hypothesis, may be equally well accounted for by the hypothesis we offer.

SUMMARY

A case is reported exhibiting varying grades of heart-block. At times there was dissociation between auricles and ventricles except for brief intervals in early ventricular diastole when auricular excitations were capable of being transmitted.

Four cases showing a somewhat similar incidence of transmission during block have been reported previously and interpreted as due to a supernormal phase in conduction.

Alternative assumptions which equally well account for phenomena observed in our case are (1) prolongation of the rest period in the critical area of block prior to transmission or (2) transient improvement of the nutrition in the area of block due to ventricular systole and increased blood flow. The latter would seem to account for the phenomena observed in all cases thus far described quite as well as the hypothesis of a supernormal phase in conduction.

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THE ABERRANT VENTRICULAR COMPLEX AS AN AID IN PROGNOSIS*

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IN 1914, E. P. Carter[1] published observations on twenty-two patients with cardiac impairment in which aberrant ventricular beats appeared in electrocardiograms, and defined an aberrant contraction as one resulting as a direct sequence of an impulse arising in a supraventricular focus, but reaching the ventricle through either unusual or partially defective channels. Such curves were characterized by: (1) a QRS wave more than 0.1 second in duration, and occupying more than one-third of the entire complex; (2) a relative increase in the amplitude of the initial deflections; (3) a T-wave opposite the main deflection; (4) notching in at least one lead, giving bizarre forms; (5) frequent exaggeration of the T-wave.

Robinson,[2] in 1916, reported studies of transient prolongation of intraventricular conduction and notching of the ventricular wave. In his opinion, these abnormal ventricular complexes were dependent on a derangement of the intraventricular conduction which prevented the passage of the excitation wave, either along the usual paths or at the usual rate through the ventricle, and which was functional in origin.

Oppenheimer and Rothschild[3] reported seventeen cases which showed the following abnormalities in the electrocardiogram: (1) abnormal prolongation of the QRS complex, with R broader and blunter than normal and separated as to footpieces; (2) notching of R; (3) low voltage; (4) absence of diphasic curves, with huge T, as in experimental bundle-branch block. Autopsies were performed on five of the seventeen cases. Four of these showed coronary arteriosclerosis with closure of the anterior descending branch of the left coronary, and all five showed a disseminated patchy sclerosis, predominating in the endocardial and subendocardial layers, and more marked in the left ventricle than in the right. In a later paper,[4] these authors used the term "intraventricular block" to mean any delay in conduction below the main stem of the bundle of His, and to include bundle-branch block and arborization, or Purkinje, block. They reported sixty-two cases of intraventricular block, four of which showed electrocardiograms typical of bundle-branch block.

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Carter,[5] in 1918, tabulated thirteen more cases with aberrant ventricular complexes, nine of them having low voltage. After study of autopsy material, he concluded that the curves with low amplitude and bizarre ventricular complexes were associated with a diffuse sclerosis of the terminal arborizations of the Purkinje system, and that the curves with large amplitude, essentially diphasic, were indicative of a totally obstructive temporary or permanent lesion of one of the branches of the atrioventricular bundle. However, F. M. Smith[6] produced extensive fibrosis of the endocardial layers of the dog, and found only one example of tracings similar to those in Oppenheimer and Rothschild's clinical studies. He later[7] concluded, after further experimental work, that there were two factors necessary for the production of an atypical QRS—cardiac fatigue and a lesion of the intraventricular conduction system. Robinson[8] sought to explain the abnormal QRS waves on the basis of functional fatigue, due to the accumulation of acid metabolites in the absence of an adequate supply of oxygen. Drury[9] reported a heart identical with those described by Oppenheimer and Rothschild, but with an electrocardiogram showing none of the findings thought by them to be indicative of arborization block.

Wilson and Herrmann, in experimental work in 1920[10] and 1921,[11] concluded that there was no evidence to show that lesions of the subdivisions of the bundle or the arborizations caused striking or characteristic changes in the electrocardiogram. They believed that the complexes described by Oppenheimer and Rothschild were due, not to an arborization block, but to an incomplete bundle-branch block, giving complexes transitional between the normal and those of complete bundle-branch block. Lewis[12] does not believe that the "arborization block" tracing of Oppenheimer and Rothschild means a particular lesion of the Purkinje network, but that it is often due to a retarded conduction in the main stem, and is associated with a grave cardiac malady like any other gross anomaly of the ventricular electrocardiogram.

Although it is not safe to be dogmatic about the origin of these aberrant complexes, it is generally recognized that any electrocardiographic evidence of departure from the normal time and pathway of conduction through the ventricle is a serious sign. In order to establish its prognostic significance, a number of studies have been made. P. D. White[13] compared the mortality rate of three groups of heart disease cases. During the same period of time, 47 per cent of the patients with heart disease and normal rhythm, 48 per cent of those with auricular fibrillation, and 100 per cent of those showing both auricular fibrillation and aberrant ventricular complexes died. In 1922[14] he made a comparison between auriculoventricular block and intraventricular block, considering the latter as including bundle-branch block and "aberration." He concluded, after a study of 286

cases, that the mortality is slightly higher in intraventricular block; that heart failure, especially of the anginal type, is more common; and that angina pectoris is four times more frequent in intraventricular than in auriculoventricular block.

Willius[15] reported a 69.6 per cent mortality rate, with an average duration of life of 8½ months, in a series of 138 patients showing the signs attributed to "arborization block" (increased width of the QRS complex, notching of the apex, or splintering of the limbs). Later, he made a study of 747 cases, over a period of 5½ years, and found that 24 per cent of those with notching and slurring in one lead only had died, while only 11 to 14 per cent of a control series of cardiac cases had died of heart disease.

In order to add to the information which is gradually accumulating on the subject of disturbances of intraventricular conduction as manifested by aberrant complexes in the electrocardiogram, a survey was made of 2693 electrocardiograms taken on 1882 patients of the University Hospital and its Out-Patient Department during the six years between January 1, 1920, and January 1, 1926. Tracings were not taken of hospital bed-patients during the latter half of this period because of poor electrical connection between the hospital and the electrocardiograph, located in the Out-Patient Department a block away, and consequently tracings of ambulatory patients are much in preponderance. A few tracings are included of referred patients about whom very little or no information is available. For this particular study all tracings showing a QRS interval definitely above 0.10 second have been collected. In most cases there have been other abnormalities in the ventricular complex, such as inversion of the T-wave or notching of the QRS group. Attempts have been made to follow the subsequent history of these patients, and all information received before June 1, 1926, is included in this report.

During this six-year period thirty-eight patients were found, by means of the electrocardiograph, to have well-marked evidence of intraventricular conduction defect. Tracings showing minor or doubtful changes have not been included. Information either as to death or the subsequent course of disease was available in twenty-seven cases. Six cases had complete records, but could be followed only a year or less after the abnormal electrocardiographic tracing was made. Five cases had neither clinical records nor subsequent reports.

CLINICAL OBSERVATIONS

Age and Sex.—Of the thirty-three patients with clinical records available, nineteen were male and fourteen female. The youngest patient was 23 and the oldest 80. Twenty-five of the total number were above 50 years of age, fourteen being between 50 and 60, and eight between

60 and 70. Two were over 70 and one was 80. Only eight were younger than 50, three of these being over 40, three over 30 and two over 23.

Onset of Symptoms.—The interval elapsing between the appearance of the first cardiac symptoms and the abnormal electrocardiographic findings varied from one month to fifteen years. This information was not obtained in all cases, and was not particularly accurate when available; however, it is interesting to note that eleven patients had complained of cardiac symptoms for a year or less, eight for from two to five years, and eight for from six to fifteen years—two of these reporting cardiac symptoms for ten years, and three for fifteen years.

Type of Symptoms.—Dyspnea was reported as a prominent symptom 25 times; precordial pain 9 times; edema, generalized or in the legs, 8 times; and palpitation 8 times. Fatigue, dizziness and indigestion occurred in a few cases and one patient, with complete heart-block, had a history of syncopal attacks.

Blood Pressure Readings.—Blood pressure readings were recorded at least once in each of twenty-six of the patients. In thirteen, the systolic reading was 150 mm. or above, going above 200 only four times. In twelve patients the systolic pressure was below 150, and below 120 only five times. The diastolic pressure was 100 or above in eight cases.

Diagnoses.—Chronic valvular disease with mitral regurgitation was noted seven times in the thirty-three cases in which a diagnosis was recorded. Cardiac hypertrophy was mentioned eleven times. Arteriosclerosis, either coronary or generalized, appeared as a diagnosis nine times. In the twenty-three-year-old patient the electrocardiogram was taken after an acute attack of tonsillitis, and there was no clinical evidence of heart disease at the time. In another patient, aged thirty-four years, syphilis was found to be present, but no clinical evidence of heart disease. Auricular fibrillation occurred seven times. Five of these patients died, four of them at an average interval of 5½ months from the time of the electrocardiographic record. Case 18 was known to have had auricular fibrillation for five years, but first showed the tracings of intraventricular conduction delay ten months prior to his death. Case 3 is working, although the heart is somewhat decompensated. He is known to have had auricular fibrillation and aberrant ventricular complexes for six years.

Mortality and Prognosis.—Of the twenty-six patients studied with subsequent follow-up reports, ten, or 38.4 per cent, were known to be alive on June 1, 1926. Two had not been heard from for a year or more. Fourteen, or 53.8 per cent, were known to have died. Case 27 died in an accident and has not been included in the figures. The date of death was reported in thirteen cases, and eleven, or 45.8 per cent lived for a year or less after the time of the discovery of the

abnormal electrocardiogram. One patient lived 1½ years (Case 15) and one for 2⅙ years (Case 11) after the electrocardiographic diagnosis. The average length of life for all thirteen patients was 8⅘ months, and for the eleven who lived a year or less, it was 6⅚ months. Of the ten patients known to have been alive when this study was completed, one with complete heart-block (Case 1) was still living 7 years after the first electrocardiographic study. Three lived for 6 years. Case 3 had auricular fibrillation, marked arteriosclerosis and a dilatation of the descending aorta at the time of his first electrocardiographic study, when he was sixty-two years old. The other two were women under thirty years of age (Cases 4 and 19), one of whom had a rheumatic valvular lesion at the time and the other developed signs of a valvular lesion later. Both have successfully gone through pregnancies since their first study. There has been no opportunity to repeat their electrocardiographic tracings in later years, although follow-up reports indicate good health. Case 20 has been taking antisyphilitic treatment. She has never had symptoms or clinical signs of heart disease and her electrocardiogram has shown a tendency to approach the normal. Cases 21 and 26 were followed for 3 and 2½ years, respectively, but could not be traced further. The others in the group of those still living had been observed from 7 months to 1½ years when this study was ended.

Fourteen of the twenty-six patients studied are dead, giving a mortality percentage of 53.8. Eleven, or 45.08 per cent, died within a year of the discovery of the abnormal complex. Seven of the ten patients who are living have lived a year or more (four of them 6 years or more) and two others are known to have been alive 2½ and 3 years after the electrocardiograms were taken. A control group of patients with auricular fibrillation was followed during the same period of time. Information was received on thirty-two of them and fifteen were reported dead, giving a mortality rate of 46.8 per cent.

Type of Death and Complications.—Information as to final illness is very incomplete except in five cases. Of the four who died in a state of congestive failure, one was found dead in bed and two had bronchopneumonia, one in combination with a thrombosis of the leg, with amputation. One, a man of thirty-one years, died after a few hours of severe substernal pain, without calling a physician.

The important complicating conditions found outside of the circulatory system were: acute tonsillitis (1); cholelithiasis, with operation (1); chronic tonsillitis with operation (2); morphinism (1); paralysis agitans (1); pernicious anemia (1); and achlorhydria (1).

Autopsies.—Three cases came to autopsy. Two hearts weighed 700 gm. each and one weighed 715 gm. Coronary sclerosis was recorded in two cases. One showed a marked aortic stenosis and another a slight

grade of thickening and contraction of the aortic valve. The muscle was described as being dark red with a yellowish tinge in one case, soft and flabby in another, and having a slight thrombosis of the left ventricle in the third.

ELECTROCARDIOGRAPHIC FINDINGS

In the thirty-eight cases studied, nine showed a preponderance of the left ventricle over the right. Six gave evidence of a right branch- and one of a left branch-block. Twenty-five showed distinct notching in the R- and S-waves of one or more derivations. Delay in the auriculoventricular conduction beyond 0.20 second occurred 6 times, including one complete and persistent heart-block and one heart-block which varied markedly in degree in different tracings, from delayed auriculoventricular conduction to partial and sometimes complete heart-block. The QRS interval varied from 0.11 to 0.17 second, with an average of 0.1327 second. In eleven cases, the QRS interval was over 0.15 second. In two patients, both of whom died, the QRS interval increased from 0.13 to 0.15 and later to 0.17 second, while under observation. Auricular fibrillation occurred eight times (once paroxysmal). Six of these patients have died. Case 3 has been observed for 6½ years. The patient with the paroxysms of fibrillation has not been traced. Extrasystoles occurred in the tracings of eleven cases—four left ventricular, three right, one right and left alternating, two ventricular, indeterminate as to side of origin, and one auricular. Five deaths have been reported in the eleven cases.

T-Waves.—In Lead I, the T-wave was inverted thirteen times, diphasic six times, and positive nineteen times. In Lead II, the T-wave was inverted five times, diphasic twice, and positive thirty-one times. In Lead III, the T-wave was negative seven times and diphasic twice. Inversion of T-wave in Leads I and II occurred only three times in combination. Only six of the fourteen cases who died showed any inversion of the T-wave. Two showed inversion in Lead I and two in Leads I and II. T was diphasic in Lead I once and in Leads I and II once.

Right bundle-branch block, as evidenced by complexes of the levogram type, with high amplitude of ventricular waves, inverted T_1 and positive T_3, was shown in six cases. In three more cases, the T-waves gave evidence of right branch-block, but the amplitude of the ventricular deflections was low. Only one patient showed the relationship of R and T suggesting a left branch-block, but this was associated with low amplitude of the ventricular complexes. In none of these cases was the amplitude in all leads 5 millimeters or less, although four cases (Cases 8, 15, 17 and 18) registered 6 millimeters or less.

SUMMARY OF CASE RECORDS

CASE 1.—Man, aged fifty years. Dyspnea, substernal pain, attacks of syncope for one year. Blood pressure 170/85 mm. Living after 7 years and able to do light work. Electrocardiogram: $R_1 = 14$; $S_1 = 8$; $R_3 = 3$; $S_3 = 21$; notched S_2. QRS = 0.15 sec. Inverted T in all leads. Complete block.

CASE 2.—Woman, aged forty-five years. Substernal pain for 8 years. Blood pressure 148/90 mm. Living and in fair condition after one year. Electrocardiogram: $R_1 = 13$; $S_1 = 2$; $R_3 = 4$; $S_3 = 7$. QRS = 0.12 sec.

CASE 3.—Man, aged fifty-two years. Dyspnea, 3 months. Blood pressure 104/82 mm. Living after six years. Working, but decompensation increasing. Arteriosclerosis, aneurysm, auricular fibrillation. Electrocardiogram: Notched R_1; $R_3 = 3$; $S_3 = 12$. QRS = 0.12 sec. T_1 inverted. Left ventricular extrasystoles. Auricular fibrillation.

CASE 4.—Woman, aged twenty-three years. Acute tonsillitis, no cardiac symptoms. Living and in excellent health 6 years later. Electrocardiogram: $R_1 = 11$; $S_1 = 8$; $R_3 = 5$; $S_3 = 0$; $T_1 = +12$; $T_2 = +9$. QRS = 11.5.

CASE 5.—Man, aged fifty years. Dyspnea. Hypertension, cardiac hypertrophy, and dilatation. Died after 6¾ months following a femoral thrombosis. Electrocardiogram: Notched R_2 and R_3. QRS = 0.12 sec. Auricular fibrillation. T_3 diphasic.

CASE 6.—Woman, aged sixty-seven years. Dyspnea for 7 months. Blood pressure 140/88 mm. Arteriosclerosis, coronary sclerosis, cholelithiasis with operation. Died after 9¼ months with increasing congestive failure. Electrocardiogram: $R_1 = 9$; $S_1 = 1$; $R_3 = 2$; $S_3 = 9$. R_1 and S_3 notched. QRS = 0.14 sec. T_1 diphasic.

CASE 7.—Man, aged eighty years. Dyspnea, edema. Cardiac hypertrophy, hydrothorax, auricular fibrillation. Died after 8½ months. Electrocardiogram: $R_1 = 7$; $S_1 = 4$; $R_3 = 8$; $S_3 = 0$. R_3 notched. QRS = 0.12 sec. T_2 notched. T_3 inverted. Left ventricular extrasystoles. Auricular fibrillation.

CASE 8.—Woman, aged fifty-three years. Dyspnea, indigestion for 10 years. Blood pressure 150/80 mm. Cardiac hypertrophy, myocardial insufficiency, infected tonsils. Died after 1¾ months, following tonsillectomy. Electrocardiogram: $R_1 = 6$; $S_1 = 2$; $R_3 = 0$; $S_3 = 6$. QRS = 0.12 sec. Notched R_1 and S_3. $T_1 = +7$; $T_2 = +9$. $T_3 = +5$. Left ventricular extrasystoles. PR = 0.15 to 0.33 sec. Marked variation from week to week.

CASE 9.—Man, aged fifty-four years. Dyspnea and weakness for 4 years. Recent stroke. Blood pressure 130/72 mm. "Myocarditis," general edema, and hydrothorax. Died after 3¾ months. Electrocardiogram: $R_1 = 11$; $S_1 = 3$; $R_3 = 2$; $S_3 = 12$. Notched S_2. QRS = 0.13 sec. Auricular fibrillation.

CASE 10.—Woman, aged fifty-three years. Palpitation, dizziness, dyspnea for 15 years. Blood pressure 204/124 mm. Diagnosis: Hypertension, cardiac hypertrophy. Living 7 months later with condition unchanged. Electrocardiogram: $R_1 = 8$; $S_1 = 4$; $R_3 = 2$; $S_3 = 11$. QRS = 0.13 sec.

CASE 11.—Woman, aged thirty-two years. Dyspnea, weakness, cough, edema for 6 years. Blood pressure 190-195/130-150 mm. Diagnosis: mitral regurgitation,

cardiac decompensation, pulmonary tuberculosis. Died after 2 years and 2¾ months. Electrocardiogram: $R_1 = 16$; $S_1 = 2$; $R_3 = 10$; $S_3 = 0$. Notched R_1, R_2 and R_3. QRS = 0.15 sec.

CASE 12.—Man, aged thirty years. Palpitation, dyspnea, dizziness for 2½ years. Blood pressure 100/80 mm. Diagnosis: mitral regurgitation, chronic infection of tonsils. Death followed an attack of sudden precordial pain one year after patient was first seen. Electrocardiogram: $R_1 = 14$; $S_1 = 3$; $R_3 = 8$; $S_3 = 8$. QRS = 0.13 to 0.15 sec. T_1 and T_2 inverted.

CASE 13.—Man, aged fifty-six years. Dyspnea, weakness, palpitation, edema for 5 years. Blood pressure 158/110. Diagnosis: arteriosclerosis, cardiac decompensation. Died after 2½ months of bronchopneumonia. (Autopsy.) Electrocardiogram: $R_1 = 9$; $S_1 = 0$; $R_3 = 3$; $S_3 = 5$. Notched R_1, S_2, and S_3. QRS = 0.17 sec. T_1 inverted. $T_2 = +6$; $T_3 = +5$. Auricular fibrillation.

CASE 14.—Woman, aged sixty years. Dyspnea and increasing weakness for 5 years. Blood pressure 135/60 mm. Diagnosis: mitral regurgitation, cardiac hypertrophy. Death reported; date not known. Electrocardiogram: $R_1 = 9$; $S_1 = 2$; $R_3 = 3$; $S_3 = 8$. QRS = 0.13 sec. Right ventricular extrasystoles.

CASE 15.—Man, aged fifty-two years. Dyspnea, weakness, cough, edema for 2 years. Blood pressure 114/84 mm. Diagnosis: Arteriosclerosis, myocardial insufficiency, morphinism. Died after 1½ years. Electrocardiogram: $R_1 = 6$; $S_1 = 2$; $S_3 = 5$. Notched R_1, R_2, and S_3. QRS = 0.15 sec. Right ventricular extrasystoles. Partial auriculoventricular block in one tracing.

CASE 16.—Man, aged sixty-five years. Dyspnea, palpitation, edema for 3 years. Blood pressure 160/120 mm. Diagnosis: arteriosclerosis, myocardial insufficiency. Died after 4¾ months. Electrocardiogram: $R_1 = 15$; $S_1 = 1$; $R_3 = 5$; $S_3 = 16$. Left ventricular preponderance. Right branch-block. QRS = 0.12 sec. T_1 and T_2 inverted.

CASE 17.—Man, aged fifty years. Diagnosis: cardiac hypertrophy. Living and in fairly good condition 10 months later. Electrocardiogram: $R_1 = 5$; $S_1 = 0$; $R_3 = 5$; $S_3 = 5$. Notched R_1. QRS = 0.12 sec. Diphasic T_1 and T_2. Inverted T_3.

CASE 18.—Man, aged fifty-eight years. Ascites, dyspnea for 10 years. Diagnosis: mitral regurgitation, adhesive pericarditis, auricular fibrillation. Had been observed for 5 years with frequent electrocardiograms, showing no aberrant ventricular complexes. Died 10 months after these findings appeared in tracings. Electrocardiogram: $R_1 = 5$; $S_1 = 5$; $R_3 = 6$; $S_3 = 0$. Notched S_1, S_2, and R_3. QRS = 0.15 sec. Auricular fibrillation.

CASE 19.—Woman, aged twenty-nine years. Palpitation, precordial pain, dyspnea for one year. Blood pressure 110/65 mm. Diagnosis: mitral regurgitation. Living after 5 years. Electrocardiogram: $R_1 = 17$; $S_1 = 8$; $R_2 = 9$; $S_3 = 0$. $T_2 = +4$; $T_3 = +6$. QRS = 0.12 sec. Diphasic T_1. PR = 0.22 sec.

CASE 20.—Woman, aged twenty-nine years. Palpitation, precordial pain, dyspnea for one year. Diagnosis: syphilis. Living after 2 years. No symptoms. Taking antisyphilitic treatment. Electrocardiogram: $R_1 = 17$; $S_1 = 2$; $R_3 = 0$; $S_3 = 9$. QRS = 0.12 sec.

CASE 21.—Woman, aged fifty-three years. Dyspnea. Blood pressure 180/125 mm. Diagnosis: hypertension, cardiac hypertrophy. Living after three years, symptoms unchanged. Electrocardiogram: $R_1 = 13$; $S_1 = 1$; $R_3 = 2$; $S_3 = 15$. Notched R_1 and S_3. Right branch-block. QRS = 0.15 sec. Diphasic T_1. Right ventricular extrasystoles.

CASE 22.—Man, aged forty-four years. Attacks of palpitation for 15 years. Blood pressure 128 mm. systolic. Diagnosis: paroxysmal tachycardia, achlorhydria, tonsillitis. Living after 3 years, condition unchanged. Electrocardiogram: $R_1 = 6$; $S_1 = 0$; $R_3 = 22$; $S_3 = 0$. QRS = 0.15 sec. PR = 0.23 sec.

CASE 23.—Man, aged forty-six years. Dyspnea, edema for 3 months. Diagnosis: hypertrophy and dilatation of heart. Passive congestion. Died after 3 weeks of bronchopneumonia. (Autopsy). Electrocardiogram: $R_1 = 11$; $S_1 = 3$; $R_3 = 2$; $S_3 = 10$. Notched S_2 and S_3. Right branch-block. QRS = 0.12 sec. T_1 inverted; $T_2 = +4$; $T_3 = +10$. Right ventricular extrasystoles.

CASE 24.—Man, aged sixty years. Dyspnea, fatigue, numbness of legs for 3 months. Blood pressure 138/80 mm. Diagnosis: pernicious anemia, aortitis, myocardial insufficiency. Living after one year. Improved. Ambulatory. Electrocardiogram: $R_1 = 9$; $S_1 = 0$; $R_3 = 6$; $S_3 = 0$. R_2 notched. QRS = 0.11 sec. Pr = 0.21 sec.

CASE 25.—Woman, aged seventy-six years. Dyspnea, fatigue. Diagnosis: arteriosclerosis. Died after one year of a stroke, following a period of decompensation. Electrocardiogram: $R_1 = 15$; $S_1 = 4$; $R_3 = 2$; $S_3 = 8$. QRS = 0.14 sec. Diphasic T_1.

CASE 26.—Man, aged sixty-eight years. Precordial pain, palpitation, dyspnea for one year. Blood pressure 142/82 mm. Diagnosis: coronary sclerosis, cardiac hypertrophy, glycosuria. Living after 2½ years, condition improved. Electrocardiogram: $R_1 = 16$; $S_1 = 4$; $R_3 = 1$; $S_3 = 10$. Notched S_1 and S_2. QRS = 0.13 sec.

CASE 27.—Man, aged fifty-five years. Substernal pressure, dyspnea for 2 years. Blood pressure 110/78 mm. Diagnosis: mitral regurgitation, cardiac hypertrophy. Died after 1½ years following an accident. Electrocardiogram: $R_1 = 10$; $S_1 = 0$; $R_3 = 0$; $S_3 = 9$. Notched R_3. QRS = 0.13 sec. T_1 inverted. Left ventricular extrasystoles.

CASE 28.—Electrocardiogram: $R_1 = 13$; $S_1 = 7$; $R_3 = 3$; $S_3 = 10$. $T_1 = +6$; $T_2 = +6$; $T_3 = -2$. QRS = 0.12 sec. PR = 0.22 sec. Auricular extrasystoles. Auricular fibrillation (paroxysmal).

CASE 29.—Electrocardiogram: $R_1 = 13$; $S_1 = 0$; $R_3 = 8$; $S_3 = 13$. Notched R_1. Right branch-block. QRS = 0.14 sec. Inverted T_1 and T_2.

CASE 30.—Electrocardiogram: $R_1 = 10$; $S_1 = 1$; $R_3 = 4$; $S_3 = 8$. QRS = 0.15 sec. Inverted T_1.

CASE 31.—Electrocardiogram: $R_1 = 10$; $S_1 = 0$; $R_3 = 3$; $S_3 = 15$. Notched R_1. QRS = 0.12 sec. T_1 inverted; $T = +6$.

CASE 32.—Electrocardiogram: $R_1 = 8$; $S_1 = 0$; $R_3 = 4$; $S_3 = 3$. Notched R_1 and R_2. QRS = 0.15 sec. Inverted T in all leads.

CASE 33.—Electrocardiogram: $R_1 = 8$; $S_1 = 4$; $R_3 = 11$; $S_3 = 3$. Notched R in all leads. QRS = 0.17 sec. Diphasic T in all leads. Ventricular extrasystoles.

CASE 34.—Electrocardiogram: $R_1 = 4$; $S_1 = 4$; $R_3 = 23$; $S_3 = 0$. Notched S_3. QRS = 0.13 sec. Auricular fibrillation.

CASE 35.—Electrocardiogram: $R_1 = 10$; $S_1 = 5$; $R_3 = 2$; $S_3 = 12$. Notched S_2 and S_3. QRS = 0.12 sec.

CASE 36.—Electrocardiogram: $R_1 = 6$; $S_1 = 0$; $R_3 = 0$; $S_3 = 9$. Notched R_3. QRS =0.12 sec.

CASE 37.—Electrocardiogram: $R_1 = 3$; $S_1 = 3$; $R_3 = 8$; $S_3 = 1$. Notched R_3. QRS = 0.13 sec.

CASE 38.—Electrocardiogram: $R_1 = 14$; $S_1 = 4$; $R_3 = 16$; $S_3 = 4$. QRS = 0.12 sec.

SUMMARY

1. Thirty-eight cases showing electrocardiographic evidence of delayed intraventricular conduction are reported, with complete clinical records in thirty-three and subsequent follow-up records in twenty-seven cases over a period of 6½ years.

2. Over three-fourths (75.7 per cent) of the patients were past fifty years of age.

3. The systolic blood pressure was above 200 mm. in four cases out of twenty-six (15 per cent), above 150 mm. in thirteen cases (50 per cent), and below 120 mm. in five cases (19 per cent). The diastolic pressure was above 100 mm. in eight cases (37 per cent).

4. Evidences of bundle-branch block were found in ten patients (26 per cent), right in nine and left in one.

5. Low voltage, 6 millimeters or less in all leads, occurred in four cases (10 per cent).

6. Notching of R- and S-waves in one or more derivations occurred in twenty-five cases (65 per cent).

7. Fourteen patients out of the twenty-six followed, or 53.8 per cent, died, as compared with 46.8 per cent of a control series of patients with auricular fibrillation and normal ventricular complexes. In eleven patients, or 45.8 per cent of the series, death occurred a year or less after the diagnosis of intraventricular delay was made, the average length of life being 8⅘ months. Six of the eight cases complicated by auricular fibrillation have died. Ten patients out of the twenty-six, or 38.4 per cent, are known to be alive, four of them having lived for 6 years or more.

8. The finding of an aberrant ventricular complex is of serious prognostic importance, but is not incompatible with a number of years of fairly active life.

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VENTRICULAR TACHYCARDIA SHOWING BI-DIRECTIONAL ELECTROCARDIOGRAMS, ASSOCIATED WITH DIGITALIS THERAPY*

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WIDESPREAD use of the electrocardiograph and intensive study of large groups of cases of heart disease have shown that tachycardia of ventricular origin is not so rare as was at first supposed.

The first case was described in 1909 by Lewis,[1] and in 1918 Robinson and Herrmann[2] were able to review only sixteen cases, ten of which they considered doubtful. In 1923 Wolferth and McMillan[3] listed twenty-four cases reported in the literature, and at the present time there are at least sixty cases on record.[4-29] Some of these may be incorrectly interpreted, but the percentage of incorrect diagnoses is now smaller than it was a few years ago. The recent article by Palmer and White[28] contains an extensive review of the literature.

The criteria on which a diagnosis of tachycardia of ventricular origin may be made, have been set forth by Robinson and Herrmann.[2] The most definite evidence of the existence of this arrhythmia is the identification of successive P-waves in the electrocardiogram, occurring at a rate less than the rate of the ventricles. The recording of the beginning and ending of a paroxysm, showing that the first complexes have the form and position of a ventricular premature contraction and that a compensatory pause follows the end of the paroxysm, is also adequate for its conclusive diagnosis. In cases of auricular fibrillation neither of these criteria is available and under these circumstances the occurrence of paroxysms of rapid regular (or nearly regular) ventricular rhythm may be interpreted as ventricular tachycardia.

An analysis of the cases previously reported shows that ventricular tachycardia occurs under several sets of conditions. It may, rarely, occur in young people or in people apparently not suffering with grave myocardial disease. Some of the patients in this group have been addicted to the excessive use of tobacco.[24, 25] The most frequent association, however, is with severe myocardial damage and coronary disease. Many patients in this group have received large doses of digitalis, particularly since the massive dosage of this drug has been widely practiced. Of the sixty cases reported twenty-five have been associated with digitalis therapy. Details of treatment are rarely

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given but apparently few of these patients received amounts in excess of the usual modern dosage. Occasionally ventricular tachycardia is seen as a terminal arrhythmia.[23, 29] House[30] has repeatedly observed this in animals after intoxication with digitalis or the allied bodies.

The object of this paper is to place on record a case of ventricular tachycardia with an unusual type of alternation in the forms of successive ventricular complexes of the electrocardiograms and to point out the frequent association of ventricular tachycardia with digitalis therapy. Eight cases of ventricular tachycardia showing bi-directional ventricular complexes are on record, reported by Schwensen,[15] Felberbaum,[16] Reid,[17] Luten,[20] and Palmer and White.[28]

CASE REPORT

The patient, a white man of seventy-six years, was admitted to the Vanderbilt University Hospital January 5, 1928. He was irrational at this time and an accurate history could not be obtained. He had been under the care of a physician for heart disease for two years and had done well until three weeks previous to admission to this hospital. At this time shortness of breath became more marked and his mental state became confused. He had received no digitalis since about December 15, 1927.

Little could be learned of his past history. He had been referred to this clinic by his private physician in 1926 and 1927 for electrocardiograms.

Examination at the time of admission showed him to be an old man, mentally confused. He was fairly well nourished. There was slight cyanosis but no pallor. He was afebrile. There was marked distension of the peripheral veins and the jugulars were particularly prominent. The chest was emphysematous, the respirations regular, and the lungs clear except for a few moist râles at the bases. The heart was difficult to outline by percussion, the borders of dullness being approximately 13 cm. to the left, and 4.5 cm. to the right, with a supracardiac dullness of 7 cm. The apex beat was in the 6th intercostal space. The sounds were feeble and no murmurs were heard. The heartbeat was completely irregular and the pulse varied in volume from beat to beat. The rate at the apex was 115 and at the wrist 85 per minute. The peripheral arteries were thickened and tortuous. The blood pressure was 130/75 mm. The abdomen was not distended, the liver's edge was felt 4 cm. below the costal border, and there was no free fluid in the abdomen. There was no edema of the extremities, scrotum, or back. Laboratory examinations revealed a negative Wassermann reaction, normal urine, and no nitrogen retention.

The diagnoses recorded at this time were general arteriosclerosis, auricular fibrillation, and cardiac insufficiency, with right ventricular failure predominating. On the second day after admission the patient experienced an acute circulatory collapse. At this time the venous distension, cyanosis, and dyspnea became much more marked, the extremities were cold and clammy, and the pulse was of poor volume and extremely irregular, with an apical rate of 150 and a radial rate of 96. Venesection was performed and, following the removal of 300 c.c. of blood, the patient was greatly improved.

Circulatory improvement continued for two days. Digitalis therapy was begun on this day. The dosage and pulse rates can be seen in Table I.

TABLE I

Day of admission		1	2	3	4	5	6	7	8	9	10	Total
Dose in grams		0.0	0.0	0.6	0.4	0.4	0.0	0.4	0.4	0.4	0.2	2.8
Rates	Apical	115	130	115	115	90	124	90	120	a.180*	180*	
										b.130*	130*	
										c. 80	80	
	Radial	85	90	72	70	70	85	70	100	a.180*	180*	
										b.130*	130*	
										c. 80	80	

*Nearly regular rhythm, other counts were made when the heart was completely irregular and are only approximate.

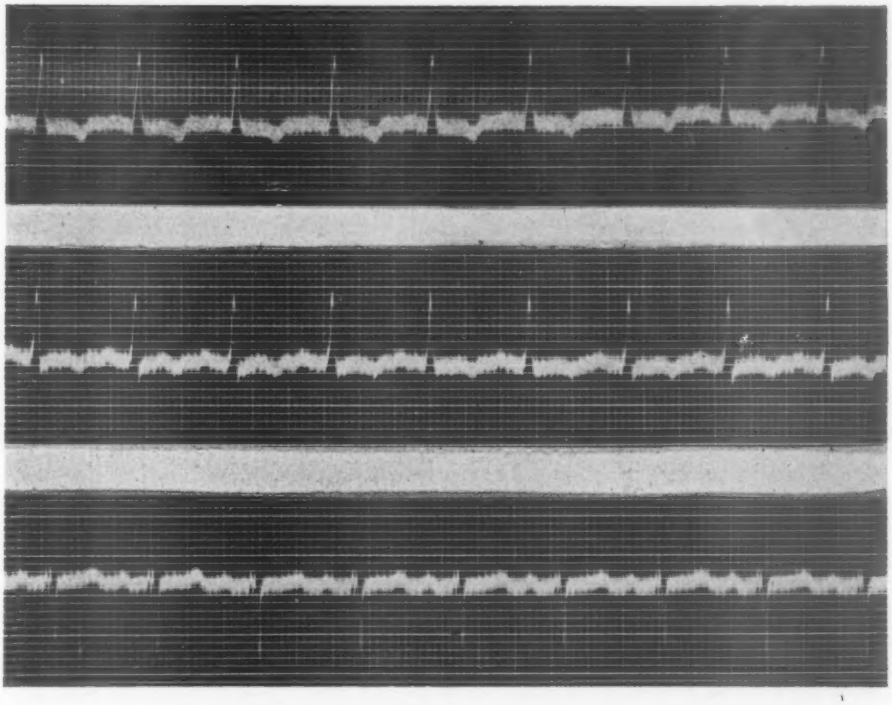

Fig. 1.

As can be seen, after the administration of 1.4 grams of digitalis, the apical rate decreased to 90 with a radial rate of 70.

On the seventh day after admission the mental state became more confused, the patient was very restless and had to be restrained in bed. Respirations became Cheyne-Stokes in character. There was then little change in his condition until the ninth day of admission. At this time there was some nausea and vomiting, the apical rate was 180, nearly regular, and with no pulse deficit, and the blood pressure was 140/100 mm. A few minutes after this observation the heart rate suddenly changed to 120 and became completely irregular again with a pulse deficit of 25. From this time on the rate changed frequently, the transition from one rhythm to another occurring either abruptly or being preceded in the electrocardiographic record by irregular ventricular ectopic beats. The rates varied from 80 to 180, the slower rate being extremely irregular with a pulse deficit, and the more rapid rates nearly regular without pulse deficit.

This remarkable succession of rhythms continued, while the general condition of the patient became much worse and he died on the tenth day of admission.

Morphine and caffein sodium benzoate at irregular intervals were the only drugs used besides digitalis.

Electrocardiographic studies: Fig. 1 represents a record made eighteen months before admission to this hospital. The heart rate is 107, the P-R interval shows a normal conduction time of 0.18 seconds. The ventricular complexes are of supraventricular origin but show a preponderance of the left ventricle. The T-wave in Leads I and II is inverted.

The patient was seen again eight months previous to admission. The record made at this time was essentially the same as that in Fig. 1.

The first record made the day after admission to this hospital is seen in Fig. 2. The rate is approximately 125, there are no regularly spaced P-waves, the waves of auricular fibrillation are present, the R-R intervals are completely irregular, and the QRS complexes are of low voltage. There is "slurring" in all leads.

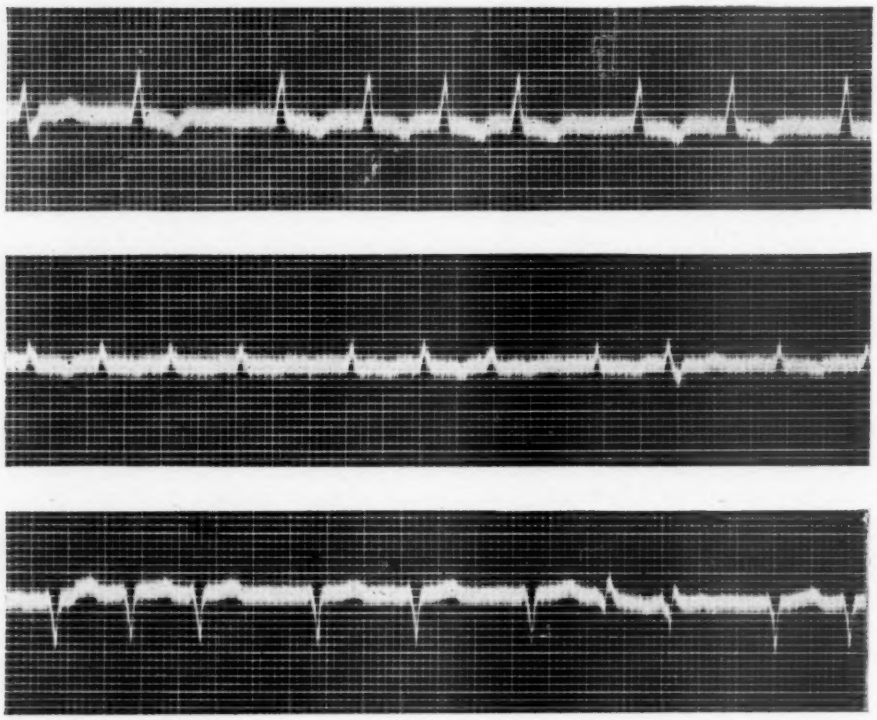

Fig. 2.

Occasional ventricular ectopic beats apparently originating both in the right and left ventricles are seen. To summarize, this record shows an auricular fibrillation with ventricular ectopic beats. The left ventricular preponderance previously noted is still present. Twenty-four hours later another record was made, which was practically identical with that in Fig. 2, except for more frequent ectopic ventricular beats.

A record made the fifth day of admission after 1.4 grams of digitalis had been given, is shown in Fig. 3. The rate has decreased to 85 per minute, and the height of the QRS complexes is less. There occasionally occur runs of three or four successive ectopic beats, although this is not shown in the record published. This suggests an increase in ventricular irritability.

Numerous electrocardiograms were made following the onset of the ventricular tachycardia on the ninth day of admission after 2.6 grams of digitalis had been

given. Three distinct types of rhythm occurred during this day. The changes from one to another were frequent and as described above, they occurred with different degrees of abruptness.

Fig. 4 shows a rate of 125 per minute, the R-R intervals are practically regular, there are no visible P-waves, the QRS complexes are not of the supra-ventricular type and approach the form of a levogram. The T-waves are upright in all leads. This is interpreted as a complete dissociation of the auricles and ventricles with the origin of an independent, practically regular, and rapid rhythm in the ventricle.

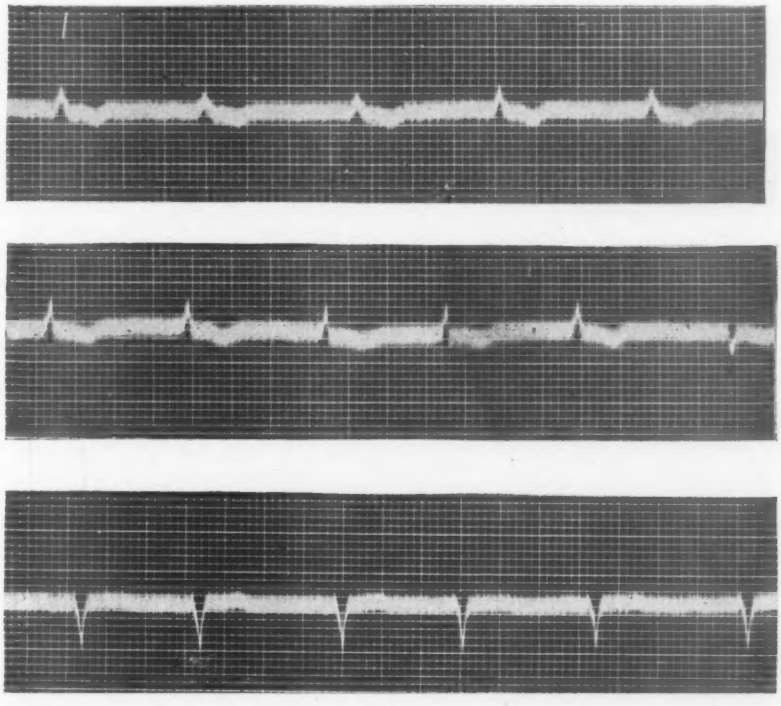

Fig. 3.

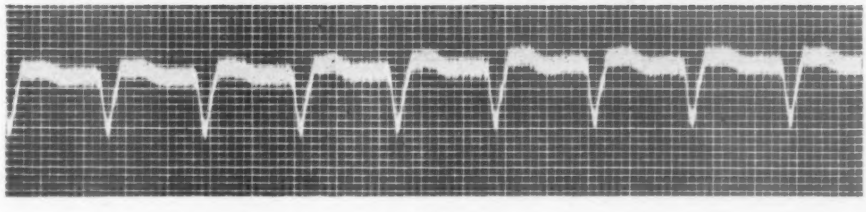

Fig. 4.

The third rhythm is shown in Fig. 5, this record shows a rate of 190 per minute. The QRS complexes are not of the supra-ventricular type, and they show an alternation of forms closely analogous to a levogram and a dextrogram. The R-R intervals show a different time relation from those described by Palmer and White.[28] They found the interval between the inverted and upright complexes longer than that occurring after the upright complexes. In the case here reported the opposite condition holds. In Leads I and II the interval from upright to inverted wave is found to be on the average 0.03 seconds longer than the

interval from inverted to upright wave. In Lead III the spacing is approximately equal. In each instance the T-waves are opposite to the main ventricular deflections.

Fig. 6 reproduces the last record made. All three types of rhythm occur within a period of five seconds. The first type seen is that described in Fig. 4, with a regular rate of 125. This is immediately followed by two ectopic ventricular beats, one originating in the right and the other in the left ventricle, and succeeding this is the type of mechanism shown in Fig. 3 with a rate of approximately 79 per minute. The next two complexes following this are ventricular ectopic beats from different foci and then the alternating type of ventricular tachycardia described in Fig. 5 is established at a rate of 156.

As exitus was approached, the changes in mechanism occurred more frequently. Death presumably was due to the onset of ventricular fibrillation.

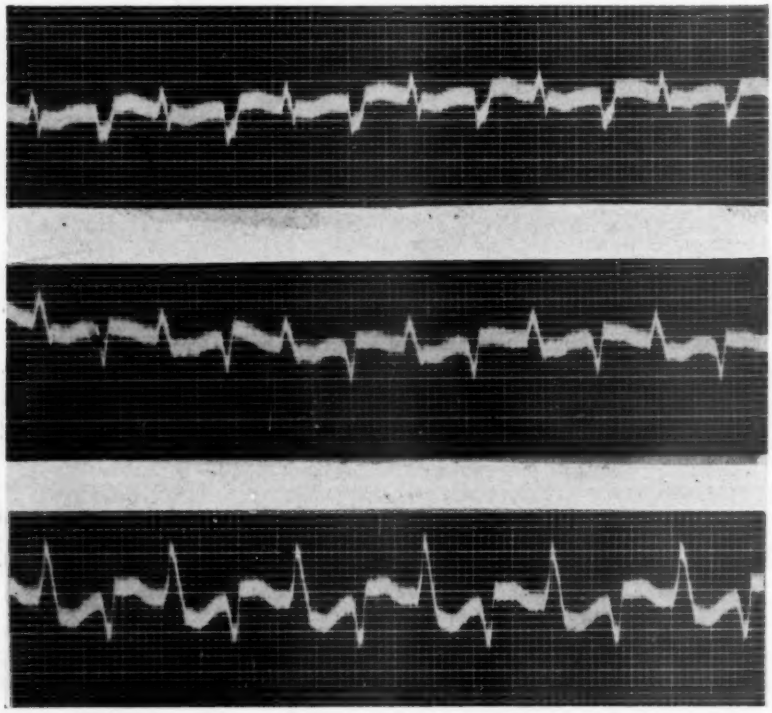

Fig. 5.

The autopsy revealed a dilated heart weighing 520 grams. The myocardium was pale and flabby, the coronary arteries were tortuous and firm but no complete occlusion was seen. On cut section silver white scars were seen throughout the myocardium. No gross lesion of the bundle of His was demonstrable. The valves were not remarkable except that the orifices were dilated. There were sclerotic patches in the aorta and the coronary openings were narrowed, the lumen of the anterior descending branch of the left coronary being about two-thirds occluded. Microscopic section showed portions of the musculature to be replaced by loose fibrils running directly into the remaining muscle cells. There was myocardial edema and considerable yellow pigment about the nuclei of the cells.

It is evident from the foregoing report that the myocardium was sufficiently damaged to interfere materially with the conduction sys-

tem and that the unusual types of rhythm were associated with severe myocardial damage. The myocardial changes were accompanied by changes in the coronary vessels.

DISCUSSION

This case presents three possible causes or conditions known to accompany ventricular tachycardia: namely, coronary disease, grave myocardial change, and digitalis therapy. Just what part digitalis played in provoking the arrhythmias in this case it is difficult to say. The patient did not receive an unusually large amount, if the time during which it was administered is taken into account. It has been suggested that digitalis may have a different action on a diseased myocardium from that on an intact one.

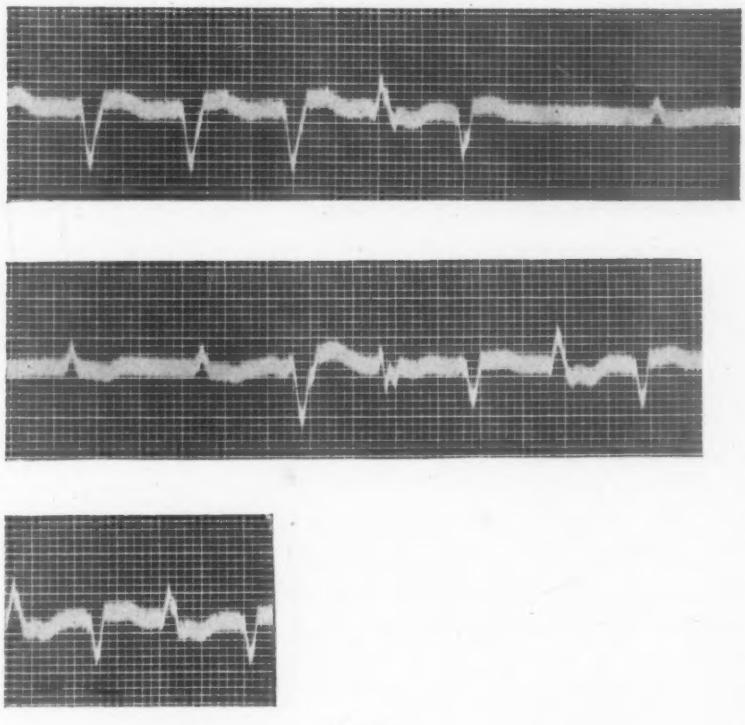

Fig. 6.

The production of abnormal rhythms by digitalis has been attributed to an increase in the irritability of the myocardium to a point of ectopic impulse formation. It is known that digitalis decreases conduction and increases excitability and contractility, and it has also been pointed out that often one or more of these effects may predominate.[13]

Gilchrist[24] suggests that differences in the response to digitalis may be due to variations in susceptibility, because of varying degrees of myocardial exhaustion, or to differences in the rate of elimination in congestive failure.

Danielopolu[13] has pointed out a definite order of onset in his cases of ventricular tachycardia produced by digitalis therapy: first an increase in the frequency of ventricular premature contractions, then the onset of bigeminy, and finally the onset of ventricular tachycardia. If the intoxication is continued, ventricular fibrillation and death may follow. These are sometimes preceded by a period of ventricular flutter. If the drug is omitted and the myocardium is capable of improving, the normal rhythm is established in the reverse order.

Otto and Gold[31, 32] have recently brought evidence to show that ventricular premature contractions, spontaneous or induced by digitalis, do not indicate susceptibility to digitalis bigeminy and that in full doses digitalis will sometimes abolish ventricular premature contractions. This diversity of opinion goes to support the assumption that the action of digitalis is a variable one. The state of nutrition of the myocardium may be an important factor in the response produced, as suggested by Edens and Huber and cited by Robinson.[33]

Palmer and White[28] in a recent report of two cases of ventricular tachycardia similar to the case here reported felt that digitalis was indicated and used it in full therapeutic doses. The rate was decreased in one and in the other was unaffected.

The same authors discuss fully the theories of the mechanism of this peculiar arrhythmia. These theories will be summarized only briefly in this paper. The two most probable mechanisms are, first, the origin of ectopic beats alternately in the two ventricles and, second, a double or figure-of-eight circus movement. Alternating bundle-branch block and parasystole have also been suggested as causes of this arrhythmia.

It has been observed that the types of auricular mechanisms associated with ventricular tachycardia are (1) normal auricular rhythm, (2) retrograde excitation, (3) auricular flutter, (4) auricular fibrillation. The latter probably occurs most frequently.

The correct diagnosis of ventricular tachycardia is important from the standpoint of therapy, for if the exciting cause is digitalis, cessation of its administration is urgently indicated. Correct diagnosis is also important from the standpoint of prognosis, as this arrhythmia most frequently occurs in advanced myocardial disease, and the mortality rate is extremely high.

Levine and Strong[34] have recently pointed out that a bedside diagnosis is possible by a very careful observation of the rhythm, which will be found slightly irregular. The quality of the first sound will also be altered. However, the only certain means of diagnosis is the electrocardiogram, and without careful study this may be misleading.

As to the treatment, the obvious course to pursue in a case provoked by digitalis is removal of the drug. This is often of no avail. Therefore, care in digitalis therapy is of great importance, and the occur-

rence of ventricular premature contractions or an increase in their number with bigeminy should be closely watched for.

Quinidine has been used in some cases with beneficial effect.

CONCLUSIONS

1. A case of ventricular tachycardia associated with digitalis administration, coronary disease, grave myocardial changes, and heart failure is reported. 2. Three types of rhythm changing rapidly from one to another are displayed in this case. 3. One of these rhythms is ventricular tachycardia displaying bi-directional electrocardiograms, adding another case to the eight found in the literature.

I wish to thank Dr. C. Sidney Burwell for his advice and assistance in preparing this paper, Dr. J. B. Hibbits, Jr., for permission to publish this case, and Dr. E. W. Goodpasture for the post-mortem findings.

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A NOTE ON THE CLEANING OF ELECTROCARDIOGRAPHIC STRINGS*

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NO PART of an electrocardiographic instrument gives more concern to the cardiologist than the galvanometer string. An extremely delicate filament, measuring only 0.003 mm. in diameter, it is subject to all the vagaries encountered in the gross manipulation of microscopic objects. Valuable and often irreplaceable electrocardiographic records are sometimes spoiled by foggy and indistinct registration of the galvanometer fiber. All electrocardiographic apparatus is or should be provided with an adequate system of lenses for focusing the shadow of the string with the greatest possible clearness; "halos" and "string cloudiness" are usually the result of improper light control.

At times, however, and especially if the string has been in use for a year or longer, the filament may become covered with a layer of microscopic dust which tends to disperse the light focused upon it. When this occurs no amount of lens adjustment can clear up the vague and indistinct edges of the shadow. Frequently, in spite of the various devices used to protect the string, larger dust particles may adhere to the filament and cast shadows which cannot be excluded by focusing. Graphic records obtained under these conditions lose much of their accuracy.

Many electrocardiographers are loath to discard their old strings, the feeling being generally prevalent that old strings acquire a certain degree of flexibility which permits the taking of better records while new strings are apt to be stiff and unresponsive. In addition, the replacement charge for new strings because of their expense, is an item for consideration.

It occurred to me about two years ago that a method of cleaning "dust-spoiled" strings might be evolved in spite of the extreme fragility of the filament and in spite of the fact that even a breath of air might rupture the fiber. In the experimental work which followed I enlisted the services of M. Albert C. Gaudin, consultant to the Boulitte Engineering Company of Paris to whom I am indebted for the extremely simplified technic described below.

A human hair not less than six inches long is prepared by immersion for twenty-four hours in a solution containing 50 per cent by volume each of ether and alcohol. The hair, free from all oil and grease, is allowed to dry by holding one end in a clean current of warm air. Having removed the electrocardiographic string from its housing in the galvanometer, it is held in the path of a strong beam of light so that it is readily visualized. The hair is then gently but firmly brushed against the filament with a downward movement, removing the hair quickly when it has reached the basal attachment of the string; this maneuver should be repeated until all sides of the string have been cleaned.

It will be found that some force can be applied to the hair without subjecting the string to any great hazard as the ether-alcohol prepared hair is much more flexible than the string. The only note of caution lies in the stroking of the string; I have found that it should be done only in a downward motion.

The method is extremely simple, requiring, however, a certain degree of dexterity which can be readily acquired by practice upon a dummy string. Strings can be cleaned several times by this method; one such, now in use at the Beth David Hospital has been cleaned four times and is over two years old.

*From The Witkin Foundation for the Study and Prevention of Heart Disease, Beth David Hospital, New York.

Department of Clinical Reports

A CASE OF AURICULAR FLUTTER WITH PAROXYSMAL ATTACKS OF 1:1 RESPONSE OF THE VENTRICLES*

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THE occurrence of 1:1 mechanism in auricular flutter (i.e., the ventricles beating at the same rate as the auricles) is sufficiently uncommon to warrant the report of an additional observation. Because of the relative frequency of auricular flutter, it is believed that paroxysms of this grade of ventricular response probably occur much more frequently than the small number of recorded observations would indicate.

A survey of the literature reveals only sixteen other cases in which this type of mechanism has been recorded. Thirteen observations in adults have been reported as follows: one by Mackenzie[1] in 1910; one by White and Stephens[2] in 1916; three by Blackford and Willius[4] in 1918; one by Scott[6] in 1922; one by MacMillan and Sweeney[7] in 1925; one by Gallavardin, Bonnamour, and Bernheim[8] in 1926; one by Allen[10] in 1927; two by Herapath[11] in 1928; one by Moore[12] in 1928; and, one by Sprague and White[13] in 1928. Koplik[3] in 1917; Lewis[5] in 1920, and Poynton and Wyllie[9] in 1926 have each reported single observations of this mechanism in children. One case of 3:2 block was recorded by MacMillan and Sweeney in which 1:1 conduction occurred in alternate cycles in a patient during exercise. The belief that 1:1 response of the ventricles in auricular flutter occurs more frequently in children than in adults[10, 14] has not been substantiated in the present survey. Only three of the sixteen recorded cases were in children.

REPORT OF CASE

W. D., a white watchman, aged forty-six years, was referred to the Heart Clinic at St. Francis Hospital on October 8, 1927, because of seizures of rapid heart action. These seizures (described by the patient as "weak spells") had appeared at least once a day during the year preceding examination. Occasionally several had occurred within one day. The attacks were abrupt in onset and in termination. Their duration varied from a few minutes to several hours. Formerly, they had appeared only after exertion or excitement, but recently many had occurred during periods of rest. Because of their increasing frequency, the patient had spent most of his time in bed during the preceding four weeks. During the attacks, the consciousness of rapid heart action would be accompanied by dyspnea, vertigo, nausea, and profuse perspiration. Flushing of the face and tremor

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†R. B. Mellon Fellow in Medicine, 1927-28.

of the hands would appear. A feeling of soreness in the region of the left nipple and occasionally along the left arm had been noticed at times. Severe, sharp pains in these areas were occasionally felt. Great distress with a feeling of utter helplessness had marked the more recent seizures. In an unusually long attack on the night before admission, dyspnea and precordial pain had been so great that the patient had feared immediate death.

Symptoms of heart failure had preceded the first attack (about one year before admission) by only a few weeks. Since then there had been a progressive increase in weakness, nervousness, and dyspnea on exertion. Between attacks the patient had been very comfortable while at rest. Occasional transient periods of paresthesia in the form of skin tenderness had appeared over the precordium, in the left shoulder region and along the left arm. The past medical history was negative for rheumatic fever, tonsillitis, chorea, scarlet fever, and venereal infections.

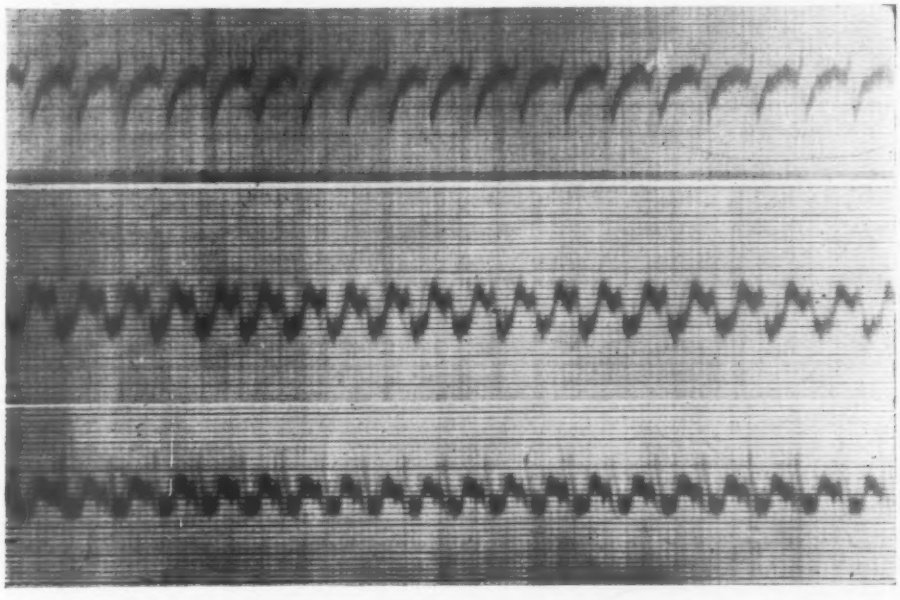

Fig. 1.—Leads I, II, and III. October 14, 1927. Electrocardiogram taken during a paroxysm of tachycardia due to 1:1 response of the ventricles in auricular flutter. Rate is 240 per minute.

At the time of his admission to the Heart Clinic, the patient was very anxious about his condition. Examination revealed many carious teeth, small atrophic tonsils, and overfilled jugular bulbs which were the seats of rapid forcible pulsations. A few small moist râles were heard over the left lower lobe posteriorly. The apex impulse was seen and felt in the 6th interspace about ½ cm. to the left of the midclavicular line. A slight systolic thrill and a soft presystolic murmur were noted in the region of the apex. The second pulmonic sound was greatly accentuated. The rhythm was regular. The rate of 120 per minute was not increased by moderate exercises and changes in posture. The blood pressure (patient seated) was 190/120 mm. The lower border of the liver was felt about 2 cm. below the costal margin.

A provisional diagnosis of auricular flutter was made, and the patient was admitted to the St. Francis Hospital on the medical service of Dr. J. D. Heard. Laboratory data included normal blood counts and urinalyses, basal metabolic rates

of +10 and +4, a negative blood Wassermann, and a roentgenogram of the chest showing an enlarged, globular heart. Either electrocardiograms or polysphygmograms were made at least once daily until after the change in mechanism had been recorded.

The auricular rate upon admission and for sixteen days thereafter was 240 per minute. Paroxysms of 1:1 response of the ventricles appeared about once a day during the first eight days of observation. Attacks varied in duration from a few minutes to approximately two hours. During the paroxysms, the patient was very apprehensive. He would lie quietly in the dorsal position, perspiring profusely, and fearing to eat or even to turn in bed. In the intervals between attacks, no symptoms were experienced. Fig. 1 shows an electrocardiogram made during one attack in which the auricular and ventricular rates were the same. At that time pressure applied over the carotid sheaths failed to produce any slowing

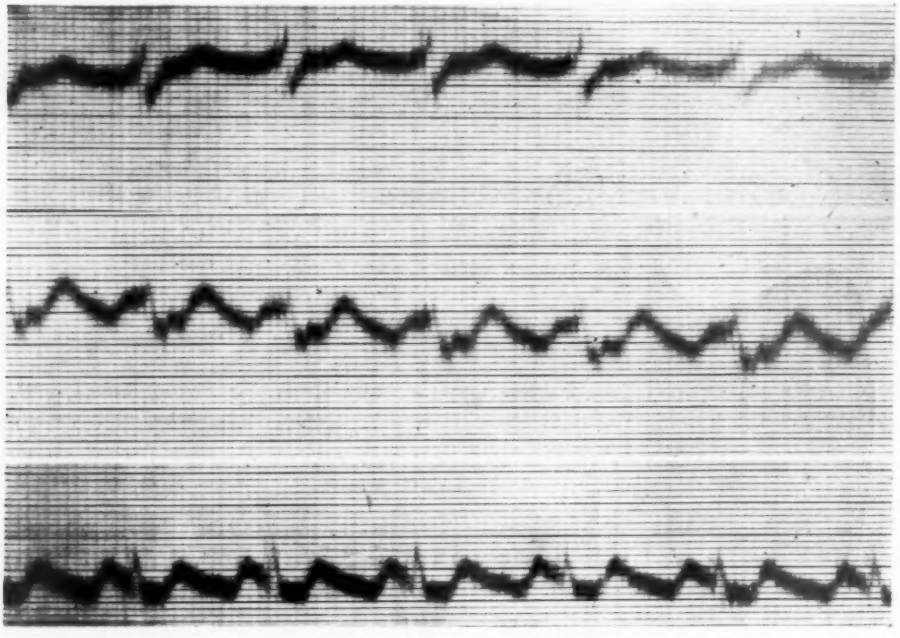

Fig. 2.—Leads I, II, and III. October 28, 1927. Electrocardiogram taken at end of first course of quinidine. Curves show auricular flutter with an auricular rate of 170 and constant 2:1 response of the ventricles.

of the ventricles. Between the paroxysms, an arrhythmia was noted, corresponding to rapid and irregular changes between 2:1 and 3:1 grades of heart-block. The rate of the ventricles varied between 100 and 120. Blood pressure readings during the period of rest in bed varied between 135 and 95 systolic and 90 and 75 diastolic. During the paroxysm of 1:1 response of the ventricles recorded in Fig. 1, readings were 110 systolic and 75 diastolic. The differences between brachial and femoral blood pressures remained within normal limits.

Digitalis was given to stabilize the degree of heart-block. After a constant 2:1 block was established, three courses of quinidine sulphate were administered. The only demonstrable effect on the heart was a slowing of the auricular rate in the first course from 240 to 170 per minute (see Fig. 2). In each course the quinidine was discontinued when signs of intolerance (dryness of the throat, nausea, and diarrhea) became severe. Digitalis was discontinued during the periods in which quinidine was given. Following the third unsuccessful attempt to change

the mechanism by the use of quinidine, the doses of tincture of digitalis were increased to a total of two drams daily. Ten days later (i.e., 5 weeks after admission), the cardiac rhythm became grossly irregular. An electrocardiogram taken at that time showed that the mechanism had changed to auricular fibrillation. The patient was discharged a few days later in a greatly improved condition.

During the six months subsequent to his discharge, the patient returned to the Heart Clinic for weekly observations. Maintenance doses of digitalis were given. Auricular fibrillation continued with a usual apex rate of about 120 and a radial rate of about 80. An electrocardiogram (see Fig. 3) made approximately five months after discharge from the hospital showed auricular fibrillation with high T-waves in Lead II and occasional multifocal ventricular extrasystoles. The

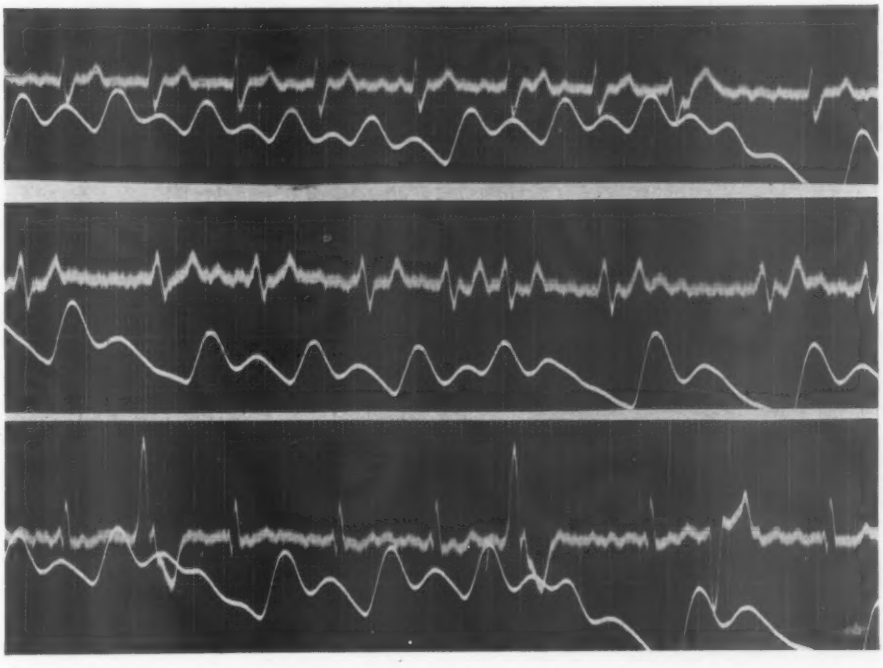

Fig. 3.—Leads I, II, and III. April 7, 1928. Electrocardiogram showing auricular fibrillation with occasional multifocal ectopic beats of ventricular origin. Arteriogram made with the cuff over the left brachial artery at a cuff pressure of 55 mm. Hg. Ventricular rate about 100 per minute.

auricular fibrillation proved to be a more favorable mechanism than auricular flutter, inasmuch as the patient remained free from the attacks of rapid heart action. He was able to carry on light work with no distressing symptoms.

SUMMARY

A total of only 16 recorded observations of 1:1 response of the ventricles in auricular flutter has been collected in a survey of the literature.

An additional report is made of this type of mechanism in an adult presenting organic heart disease.

In this case digitalis prevented the occurrence of paroxysms of 1:1 response of the ventricles. Three intensive courses of quinidine

failed to produce any changes in mechanism. A change to auricular fibrillation finally appeared while the patient was receiving large doses of digitalis.

The mechanism of auricular fibrillation continuing over a period of several months was proved to be more favorable than that of auricular flutter.

I am indebted to Dr. J. B. Heard for his suggestions and for permission to report this case.

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Department of Reviews and Abstracts

Selected Abstracts

Richards, Dickinson W. Jr., and Strauss, Marjorie L.: Circulatory Adjustment in Anemia. Jour. Clin. Invest., 1928, v, 161.

The present investigation is a study of the cardiac output in eight anemic subjects both during the stage of anemia and at intervals in the period of recovery. Two were suffering from primary anemia, four from secondary anemia following hemorrhage from gastric or duodenal ulcer, one from secondary anemia with cacinoma of the stomach and one had a secondary anemia associated with purpuric manifestations. When the experiments were made, the subjects were in all instances apparently well compensated to their anemia.

The data which were measured in each experiment were: (1) alveolar and oxygenated "mixed venous" CO_2 tensions, (2) minute volume and O_2 and CO_2 percentages of expired air, (3) CO_2 dissociation curve of venous blood, (4) oxygen capacity of venous blood.

From these data were calculated: (5) cardiac output per minute (Field-Bock method), (6) arterial and venous serum pH, (7) oxygen consumed per 100 c.c. of blood (8) oxygen consumed per cent of capacity, (9) basal metabolic rate and, (10) respiratory quotient.

In this series of patients, there was a tendency for the following changes:

a. Increased cardiac output.
b. Increased percentage utilization of oxygen by the tissues.
c. Decreased utilization of oxygen by the tissues in cubic centimeters per 100 c.c. of blood.
d. In five instances, a relative increase in metabolic rate during severe anemia.
e. Low respiratory quotient; frequently this increased during recovery from anemia.
f. Increased ΔpH (difference between arterial and venous serum pH).

Of these changes, (c), (e), and (f), are shown to be consistent with the change in form of the CO_2 dissociation curve in anemia. A balanced relationship between cardiac output (a) and the percentage of oxygen (b) is possible, on the basis of vasomotor dilatation and lowered blood pressure in the anemic state. Blood pressure has been reported as lowered in anemia; vasomotor dilatation is to be expected when, as here, mean capillary or tissue oxygen tension is decreased.

Katz, Louis N., Ralli, Elaine P., and Cheer, Sheo-Nan: The Cardiodynamic Changes in the Aorta and Left Ventricle Due to Stenosis of the Aorta. Jour. Clin. Invest., 1928, v, 205.

The authors have studied the dynamic changes that occur in stenosis of the aorta, using optically recording manometers of high efficiency, recording simultaneously the pressures within the aorta and the left ventricle.

Dogs were used in the experiment. Stenosis of the aorta was produced by tightening a ligature around the aorta, using a specially designed screw arrangement for this purpose. The experiments were made under various conditions of arterial resistance, venous return and heart rate. The rate of alveolar CO_2 was maintained constant during each experiment. The vagi were cut in most cases; in a few, however, they were left intact.

The experiments were different from clinical conditions of aortic stenosis in that the ventricular hypertrophy, aortic insufficiency and myocardial involvement which usually complicate the clinical cases were often absent in these experiments. Since the authors have as their objects the evaluation of the primary dynamic changes in the stenosis of the aorta, they have felt that these experimental conditions might prove a clearer idea of the manner in which the clinical picture is eventually produced.

The contour of the left ventricular curve is altered by stenosis of the aorta. Its height is increased. Its summit becomes more peaked as the contraction becomes more isometric; at the same time its duration is increased and the ascent and descent are steeper. The normal parallelism in the fundamental contour of the aortic and left ventricular curves during the ejection period disappears when a stenosis is created. The amplitude of the curves as well as the gradients of the ascent, change in opposite directions and the peaks no longer coincide in time.

The changes in the aortic pressure curve produced by stenosis are summarized as follows:

a. Decreased pulse amplitude.
b. Lowered level of the pressures.
c. Prolongation of the ejection period.
d. Diminished gradient of the ascent.
e. Less decisive incisura with obscuring of its after-vibration.
f. Superimposition of systolic and early diastolic vibrations on the curve.
g. The appearance of a sharp vibration low down on the ascent of the curve.

The resemblance of the aortic curve to optical curves recorded from the subclavian artery in clinical cases of aortic stenosis is evident.

Eyster, J. A. E.: Determination of Cardiac Hypertrophy by Roentgen-Ray Methods. Arch. Int. Med., 1928, xli, 227.

The present study is concerned with an attempt to evaluate the introduction of other measurements of orthographic silhouettes and of other body measurements in relation to the prediction of the size of the normal heart and the separation of normal and hypertrophied hearts. The measurements of the silhouettes studied were the area of greatest transverse diameter of the silhouette of the lateral plane, combined with similar measurements from the frontal plane. The additional body measurements introduced were the anteroposterior and lateral diameters and the girth of the thorax. A new series of 100 carefully selected normal persons was studied and compared with 100 patients with organic heart disease. So far as this method is able to separate normal from pathologic cases, it appears obvious that the area of transverse diameter of the frontal plane predicted from age, height and weight is of definite value and that little if anything is gained by the introduction of other cardiac or body measurements. Measurements from the silhouette of the lateral plane appear to improve slightly the prediction in normal cases but the separation from the pathologic is less. The probable reason for this is that the true measurement of the transverse diameter of the silhouette of the lateral plane is not obtained in enlargement of the left ventricle, because the posterior cardiac

contour is displaced dorsally and fuses with the shadow of the spinal column, resulting in an obliteration of the retrocardiac space. This measurement, which it is possible to make accurately in the normal subject, thus is probably underestimated in most of the pathologic cases.

The author concludes that the transverse diameter of the silhouette of the frontal plane (orthodiagraphic or teleroentgenographic) similarly predicted or determined from the ratio $\frac{\text{Thoracic Girth}}{\text{Transverse Diameter of the Heart}}$ represents what appears to be the next most valuable method for differentiation.

Chang, H. C., and Harrop, George A. Jr.: The Determination of the Circulating Blood Volume with Carbon Monoxid. Jour. Clin. Invest., 1928, v, 393.

A method for the estimation of the circulating blood volume in man is described. It consists in the inhalation of a measured amount of carbon monoxid and the subsequent estimation of its concentration in the circulating blood. The maximal error in the technical procedures involved does not exceed five per cent.

The circulating blood volume has been found by this method in sixteen normal individuals to lie between 60.4 and 75.5 c.c. per kilogram of body weight.

The circulating blood volume when expressed as cubic centimeters per square meter of body surface in these individuals varied between 1990 and 2860 c.c.

The sources of error of the carbon monoxid method are discussed and the probable reasons are stated for the discrepancies in the results as compared with those of the dye method.

Derick, Clifford L., Hitchcock, Charles H., Swift, Homer F.: The Effect of Anti-Rheumatic Drugs on the Arthritis and Immune Body Production in Serum Disease. Jour. Clin. Invest., 1928, v, 427.

1. If, immediately following the discontinuance of serum therapy, neocinchophen or aspirin in adequate dosage is given to patients and continued throughout the usual period of serum disease, arthritis is usually prevented even though other manifestations of serum disease occur.

2. The serum of patients treated in this manner usually fails to contain anti-horse serum precipitin, and only rarely shows a precipitin concentration above 1:40.

3. Usually a precipitin content of 1:400 is necessary before the patient shows arthritis.

4. The theory is advanced that urticaria in serum disease is the result of active sensitization of the skin which is not prevented by the drug treatment, while the arthritis is the result of passive sensitization of the joints which is inhibited when the circulating antibodies in the serum are kept to a low concentration by the anti-rheumatic drugs.

Fahr, George: Hypertension Heart. Am. Jour. Med. Sci., 1928, clxxv, 453.

In this address, the author deals extensively and carefully with present day knowledge concerning this very important subject. It should be of interest to those dealing with patients of this type.

The author states that approximately 140,000 persons in the United States die each year from the consequences of high blood pressure. The widespread prevalence of this condition, therefore, should concern us all.

Willius, Frederick A.: Clinical and Pathologic Data in Cases Exhibiting T-wave Negativity in the Electrocardiograms. Am. Jour. Med. Sci., 1928, clxxv, 630.

This study comprises 130 cases in which the electrocardiograms showed T-wave negativity other than in Lead III alone and in which necropsy was performed. Clinical data in conjunction with pathological changes found at necropsy are presented. The clinical types of cardiac disease were numerous, but hypertensive cardiac disease and coronary disease occurred with greatest frequency. Significant sclerosis of the coronary arteries was demonstrated at necropsy in 40 per cent of the cases.

White, Paul D.: The Clinical Significance of Gallop Rhythm. Arch. Int. Med., 1928, xxxxi, 1.

The author reports a series of patients with gallop rhythm observed during the last few years in private and hospital practice. He points out the difficulty of differentiating this phenomena into various types. With rapid heart rates, the position of the third sound is often difficult to place. He feels that the commonest type, namely, the protodiastolic is probably due to the marked accentuation of the usually faint normal third heart sound.

Gallop rhythm is almost invariably evidence of serious heart disease. Almost half of the one hundred patients under observation are known to have died within two years of the discovery of the sign. A considerable number of those remaining were seriously ill or dead when last heard from.

Primary disease alone, or in combination with other conditions was apparently present in more than one-half the cases. Congestive heart failure was the most outstanding feature of the heart disease, being present in at least 61 per cent. Angina pectoris was also a common occurrence. Pulsus alternans was frequently found.

Electrocardiograms were obtained in 64 of the patients. Only two of these were normal. Intraventricular block was the most common electrocardiographic abnormality found, occurring in 24 cases. Auriculoventricular block was surprisingly infrequent being recorded in only eleven cases.

The author discusses the possible explanation for the occurrence of this phenomenon.

Bramwell, J. Crighton and Duguid, J. B.: Aneurysmal Dilatation of the Left Auricle. Quart. Jour. Med., 1928, xxi, 187.

The authors report two cases of chronic rheumatic carditis showing marked enlargement of the heart that were studied at autopsy. In one the heart was enlarged so much that it occupied the whole lower part of the right lung and gave rise to an extensive area of dullness in the back. The marked increase in size of the heart was caused by a greatly dilated left auricle. The other chambers of the heart showed the customary thickening and dilatation seen in such specimens.

Examination of the wall of the auricle showed extensive destruction of muscle tissue and replacement by fibrous tissue. It was the place of greatest fibrosis that the auricle showed dilatation. For this reason, the authors choose to describe the process as aneurysmal dilatation of the auricles.

Both cases showed some pericardial involvement. This was not extensive. The adhesions were more apt to be found over the region of the fibrosis. They feel that the pericarditis was not a factor in the production of the dilatation.

The surprising feature of these patients is the comparative well being for several years after this extensive cardiac damage had been established. It is suggested that this can be explained by the fact that the brunt of the damage is borne by the auricle, whereas the muscle of the ventricle remains relatively healthy and indeed often exhibits considerable hypertrophy.

Howard, C. P.: Aortic Insufficiency Due to Rupture by Strain of a Normal Aortic Valve. Canadian Med. Assn. Jour., 1928, xix, 12.

A man aged thirty-three years, chauffeur by occupation, complained of sharp pain in the left upper chest and in the epigastrium following a severe exertion. He became short of breath and began to cough. Later the pain became severe enough to cause him to discontinue work. He died in the hospital three months later. The post-mortem examination showed that the common attachment of the anterior and medial (left posterior) cusps of the aortic valve was drawn away from the aortic wall, due to a transverse tear in the intima five-eighths of an inch in length, allowing the cusps to become very lax. There was a fairly extensive sclerosis in the sinus of Valsalva and a still earlier process in the root and arch of the aorta, as well as the descending aorta. The heart weighed 640 grams and showed marked hypertrophy with dilatation of the left ventricle and great dilatation of the right. Microscopically the aortic cusp was normal. The vasa vasorum of the aorta showed no evidence of syphilis.

The author has collected from the literature 112 cases. He discusses the incidence of this comparatively rare accident, classifying the cases and then discusses at some length the pathogenesis, pathology and symptomatology of the group.

Levine, Samuel A.: Some Unproved Impressions Concerning the Subject of Heart Disease. New England Jour. Med., 1928, cxcviii, 885.

The author describes briefly certain impressions which he has formed after observing a great variety of patients suffering from heart disease. One of these impressions is that children suffering from rheumatic fever often show repeated epistaxis and attacks of painless nausea and vomiting. These symptoms have not seemed to bear any relationship to the more outspoken evidence of rheumatic infection, namely, polyarthritis or active chorea.

He has been impressed with the importance of the familial factor in various kinds of heart disease and feels that there are individuals who inherit a general vulnerability to vascular disease either infectious or degenerative.

Another striking phenomenon that occurs in one of the important types of heart disease that needs explanation is the great frequency with which the identical blood vessel is involved in cases of coronary thrombosis. It is furthermore quite remarkable how commonly a particular part of this vessel is involved.

He points out certain incompatibilities between common conditions that are difficult to explain. The first is the apparent antagonism between auricular fibrillation and angina pectoris. The previous existence of auricular fibrillation, even when the compensation has been well established is a real protection against the development of angina pectoris. The second incompatibility is the one that exists between congestive heart failure and fibrillation on the one hand and the development of subacute bacterial endocarditis on the other hand. The author draws attention to the fact that although mitral stenosis is the most common type of rheumatic valve disease, yet bacterial endocarditis more frequently develops in patients who have had aortic insufficiency than in those who have had mitral stenosis. The third antagonism that seems to exist is the comparative freedom from tuberculosis of the lungs in certain types of heart patients.

The author also believes that the evidence in favor of the beneficial effects of athletics upon the circulation is very meager. Certain muscles in the body may be strained by exercise, but he finds no proof that the strength or health of the circulation is similarly improved.

Orr, James: The Assessment of Cardiac Murmurs. Canadian Med. Assn. Jour., 1928, xix, 7.

This interesting subject is again brought up for discussion. The author uses the classification adopted by Mackenzie of physiological, functional and organic murmurs. He then proceeds to discuss the application of murmurs occurring in different times of the cardiac cycle and different locations on the chest wall.

Campagna, Maurice, and Hauser, Geo. H.: A Malignant Condition of the Pericardium. Jour. Am. Med. Assn., 1928, xc, 1362.

This case report is that of a white man, aged forty-two, with carcinoma of the pericardium. The unusual features were metastases, involvement of the parietal and visceral pericardium with obliteration of the pericardial cavity and no involvement of the myocardium. The tumor, an epidermoid carcinoma, arose primarily in the scalp with metastases to the cervical, mediastinal and bronchial lymph glands, left lung and pericardium.

From a clinical standpoint, a malignant condition of the pericardium, like chronic pericarditis, is almost impossible of ante-mortem diagnosis, unless associated with acute pericarditis. A review of the available literature shows that malignant disease of the pericardium is practically always metastatic whereas the primary growths of this structure are benign and very often cystic in character.

Bungartz, Thekla, and Dressen, Hans: On the Importance of the Electrocardiograph in the Heart Disease of Children. Monatsch. f. Kinderheilkunde, 1928, xxxviii, 202.

The authors describe a case of aortic stenosis occurring in a child who had signs of brain embolism. The electrocardiogram showed a right bundle-branch block. The differential diagnosis between the electrocardiogram of uncomplicated hypertrophy of the left heart and right branch block is discussed.

The value of the differential diagnosis lies in the unfavorable prognosis in the latter lesion. This was shown by the progressive downward course of the case cited where the lesion was considered to be embolic in nature.

McSweeney, C. J.: Acute Rheumatism in Childhood. Lancet, 1928, i, 959.

During 1927 an inquiry was made into the factors associated with rheumatic infection among 214 Cardiff school children who presented positive and unequivocal evidence of rheumatic infection. A control group of 116 children who had no evidence of rheumatism and who had no affection of the heart was also examined. These children were selected at random and were all of school age.

No significant differences as to the size of tonsils or frequency of sore throats were found to exist when the two groups of children were compared. Chorea, permanent heart disease or other rheumatic manifestations were found to have developed in several cases after tonsillectomy had been performed.

Some slight evidence was found in this inquiry to support the theory of the infectivity of rheumatism; 661 children were exposed to rheumatic infection by living in the same house with sick children; 51 of these contacts were affected.

Overcrowding did not seem to predispose to the onset of rheumatism, but 13 of the 214 rheumatic children found living under overcrowded conditions showed evidence of cardiac involvement. No other significant differences were noted when the social factors of the two groups were considered.

The incidence of dampness in the houses of 201 rheumatic children was not significantly higher than in the houses of 108 of the non-rheumatic children. Ground floor dampness was found to exist more often in the houses of rheumatics than in those occupied by the controls, but this did not seem to produce a tendency toward any particular type of rheumatic onset. A general dampness of the houses was more often associated with the onset of rheumatic pains than other types of onset, but the differences were not significant. Dampness of houses of whatever distribution did not appear to predispose to the onset of chorea in preference to any other type of onset. Living in damp houses did not predispose especially to rheumatic fever and to cardiac involvement. The author points out that these observations do not coincide with the findings of the B. M. A. Subcommittee, which consider that the disease of rheumatism is essentially one of children living in damp rooms.

Schlesinger, Bernard: Subacute Infective Endocarditis in Childhood. Brit Jour Child. Dis., 1928, xxv, 33.

This report represents a study of 14 children who died with evidence of subacute bacterial endocarditis. Acute or subacute rheumatism occurred some years previously in only 6 cases. A congenital malformation of the heart was present in two, while the remaining six, hitherto healthy, developed the disease insidiously with joint pains suggesting at first a simple rheumatic endocarditis.

During the last 65 years at the Hospital for Sick Children, Great Ormond Street, London, only 10 true examples of this disease were found at autopsy, as compared with 349 post-mortems on undoubted cases of rheumatic carditis with endocarditis over the same period. The author shows in two tables a comparison of the incidence of clinical signs in rheumatic carditis and subacute infective endocarditis.

He points out that splenomegalia can occur both in rheumatic carditis and in subacute infective endocarditis. Rheumatic cases belonging to this category mostly showed a large, friable, soft spleen at autopsy, a condition commonly seen in children with fatal infections. On rare occasions when splenic infarcts were observed, other signs of secondary infection were present. In subacute infective endocarditis, however, splenic infarction was the rule and was noted almost invariably in the present series.

Acute, nonsuppurative pericarditis is a very uncommon complication of subacute infective endocarditis. In fourteen autopsies on children in this series, 11 were found to have no signs of pericarditis; of the other three one showed evidences of an old rheumatic pericardial infection, the second had terminated with a purulent pericarditis and the third proved the exception with a fairly recent fibrinous infection of the pericardial sac.

From these investigations, it would appear that the pathogenesis of subacute infective endocarditis and of rheumatism is not identical, for if subacute infective endocarditis were a malignant form of rheumatism, one would expect it to be at least as common in children as it is in adults, since children are particularly susceptible to all forms of rheumatism. Similarly, if the two diseases are to be regarded as etiologically the same, it is difficult to explain why the pericardium should continually remain unaffected in subacute infective endocarditis when it is so often the seat of repeated inflammation in rheumatism. Thus if subacute infective endocarditis were simply the reawakening of a dormant rheumatic infection, one would have to suppose this infection capable of causing pericarditis in the first instance, although powerless to do so when the disease assumes a malignant form.

Davison, Hal M., and Thoroughman, J. C.: A Study of Heart Disease in the Negro Race. South. Med. Jour., 1928, xxi, 464.

A selected series of patients with heart disease admitted to the medical wards of Emory University Division of Grady Hospital from January 1, 1926 to September 15, 1927, has been tabulated and studied as to incidence, etiology, duration and mortality.

This series consists of 257 patients representing 277 admissions. During the same period there were 7,500 general admissions, of which 3.7 per cent were due to heart disease. Admissions to the male and female medical wards during this period total 1,222 cases. Of this number 265, or 21.7 per cent, were due to heart disease. Admissions to the male medical ward were 683. Of this number 175, or 24.9 per cent, were due to heart disease. Admissions to the female medical ward were 539. Of this number 95, or 17.6 per cent, of the admissions were due to heart disease. Of the 277 cardiac admissions 10 were admitted to the pediatric service. On this service during the period of study, there were 462 medical admissions. The ten cases represent 2.1 per cent of the admissions on this service.

The largest percentage of admissions occurred in the fifth decade of life and total 30 per cent. The total of all the rheumatic groups numbered 18 cases or 17.1 per cent. The largest group of cases in this series is associated etiologically with arteriosclerosis and hypertension, and numbers 71 or 27.6 per cent. However, if all cases with arteriosclerosis, hypertension, and its various complications, are grouped together, there shows a total of 157 cases or 61 per cent of the entire series.

Syphilitic heart disease causes the greatest amount of disability next to the arteriosclerotic group.

The disability from heart disease is greatest and requires longest hospitalization in the arteriosclerotic group than any other.

The mortality is unusually high, because of the marked state of congestive heart failure in which these patients are received.

Harris, L.: Syphilis of the Heart. Brit. Med. Jour., 1928, i, 840.

This paper is based on 100 cases of syphilis of the heart taken from patients attending the Liverpool Heart Hospital. They represent about 9 per cent of all cases at this institution.

The author describes the clinical evidence of cardiac syphilis, analyzing the symptoms and diagnostic signs by which this condition may be recognized. He points out the fact that the aortic valve is usually involved in these cases and that frequently there is an aortitis.

Kohan, B. A., and Bunin, C. F.: On the Differential Diagnosis of the Thrombus of the Right and Left Coronary Vessels in Living Man. Ztschr. f. Kreislaufforschg., 1928, vii, 199.

A case is described in which the diagnosis of thrombosis of the right coronary vessel was made while the patient was alive. In contrast with the symptoms of an attack of angina pectoris, such cases show sudden status anginosis with repeated protracted attacks of stenocardia and acute weakness of the heart. This is considered as the characteristic symptom of thrombosis of the coronary vessels. If the right artery is blocked by a thrombus a dilatation of the heart to the right and an acute swelling of the liver is present. The block of the left artery causes a dilatation of the heart to the left and edema of the lungs. The symptoms of right coronary thrombosis were present in the patient. The diagnosis was confirmed by autopsy.

Conference on Rheumatic Diseases. Brit. Med. Jour., 1928, i, 852.

The conference on rheumatic diseases which took place at Bath, England, May 10 and 11, 1928, is reviewed in this report. Short abstracts of the various papers read are contained in the report. The medical papers contain much of interest concerning acute rheumatic fever and the heart disease that may be associated with this infection.

Ionescu, D., and Enachescu, M.: Investigation in Mammalians and Men on Heart Nerves Coming From the Thoracic Part of the Sympathicus Below the Ganglion Stellatum. (Nervi Cardiaci Thoracales.) Zeitschrift f. Anat. u. Entwicklungsgeschichte, 1928, lxxxv, 476.

In calves and sheep one can follow without great difficulty nerve fibers which have their origin below the ganglion stellatum of the thoracic part of the sympathicus (ganglion 2-5). Those fibers frequently have anastomoses with branches of the vagal nerve and the upper sympathetic heart nerves. They were studied in human fetuses and two adults. The fibers can be followed to the heart and aorta, in most of the cases only to the auricles but sometimes to the ventricles. The left ventricle has a better supply than the right, frequently getting nerves from the right side too. The name nervi cardiaci thoracales is proposed for those nerves.

Ionescu, D., Teitel-Bernard, A., Iliescu, C., and Enachescu, M.: On the Functions of the Sympathetic Thoracic Heart Nerves. Pflüger's Archiv, 1928, ccxix, 47.

In dogs, sheep and calves the function of the nervi cardiaci thoracales was investigated. With narcosis and artificial respiration, all the other sympathetic nerves which innervate the heart were cut and an electrical stimulation of the cardiac end of the nervi cardiaci thoracales resulted in an acceleration of the pulse, an initial rise followed by a lowering of the blood pressure. This effect is the same as in the stimulation of the other sympathetic heart nerves. After removal of the ganglion stellatum a chemical or mechanical irritation of the epicardium and the aorta continues to produce a sensation of pain, which is no longer present after extirpation of the pars thoracales of the sympathicus. The conclusion was drawn that the thoracic heart nerves contain accelerating and sensory fibers, which is of importance for the removal of the ganglion stellatum in angina pectoris.

Ionescu, D.: Experimental Contribution to the Knowledge of the Sensory Cardio-Aortic Tracts. Ztschr. f. Klin. Med., 1928, vii, 415.

Experiments in cats and dogs showed that after bilateral resection of the rami communicantes C_8–D_1 and the thoracic sympathicus up to the sixth ganglion, mechanical and chemical irritation of the epicardium and the aorta no longer produces sensations of pain. The conclusion was drawn that the vagal nerve with the depressor nerve, the cervical sympathetic and the vertebral nerve cannot be considered as sensory nerves of the heart. Only by way of the nervi cardiac. infer., ganglion stellat., nerv. card. thorac., the thoracic sympathetic nerve and the rami communicantes C_8–D_5 can sensations be transmitted to the cerebrum. In men, after Leriche's experiments, communication between the vagus sympathicus, the gangl. cervic. super and the vagal nerve seem to contain sensory fibers for the heart.

Ionescu, D.: On the Pathogenesis and the Surgical Treatment of Angina Pectoris. Ztschr. f. Klin. Med., 1928, cvii, 427.

The author describes the symptoms and theories on the pathogenesis of angina pectoris. After his opinion, the pain of the attack of angina pectoris is damaged by a disease of the coronary vessels, produced by an unphysiological activity of the heart and due to fatigue of the heart muscle. Psychic or somatic stimuli may be the factors which directly or reflexly lead to an attack, the severity of which depends on the blood supply of the heart muscle. After discussion of the different surgical methods of treatment of angina pectoris, he recommends the extirpation of the ganglion stellatum. He sees the chief effect of the operation in the removal of the centrifugal impulses which force the heart to unphysiological work. After the experimental work of Ionescu in animals and his experience in man the extirpation of the ganglion stellatum does not damage the function of the heart, so far as the electrocardiogram is concerned. After the extirpation of the Ganglion stellatum, the nervi card. thorac. provide the heart with accelerative impulses to a sufficient amount. A statistical comparison with the results of other operative methods for the treatment of angina pectoris showed that its results are fairly satisfactory.

Eckerson, Lowell B., Roberts, G. H., and Howard, Tasker: Thoracic Pain Persisting After Coronary Thrombosis. Jour. Am. Med. Assn., 1928, xc, 1780.

Among 23 patients with coronary thrombosis included in this series, 12 survived the first attack. Among these 12 patients there were 4 who complained of this type of pain for various periods of time. Several of the patients in the series complained of painful attacks both before and after coronary thrombosis and others suffered from painful attacks before thrombosis who had no pain afterward.

The exact mechanism is not clear in the case of either type of pain. It seems probable, however, that (1) in the case of those who have pain only after the thrombosis, the pain is due to the infarct or its scar; (2) in those whose painful attacks cease after a thrombosis, the pain is dependent on a narrowed coronary vessel, with intermittent vessel spasm probably superadded, and (3) in those who have painful attacks both before and after coronary thrombosis, both of these factors are involved, or else more than one coronary branch is sufficiently affected to be the cause of painful attacks.

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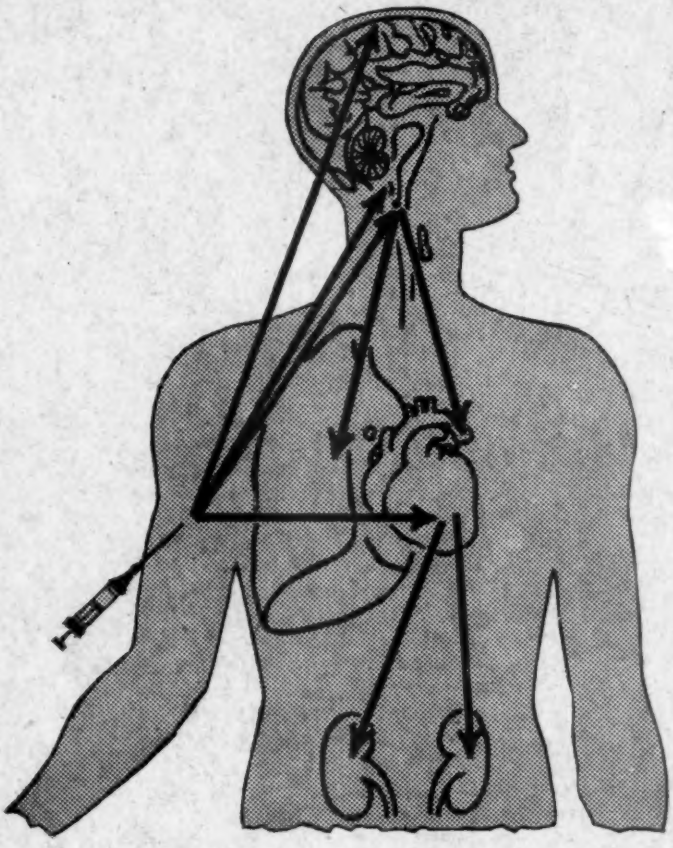

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